BRAIN.

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RÉFLEXES DE DÉFENSE.[1]

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Messieurs,—J'ai entendu raconter l'anecdote suivante: le grand seigneur espagnol auquel Cervantes a dédié son livre "Don Quichotte," voyageant en France arrive à une heure tardive dans une localité où il se propose de passer la nuit. Il sonne à une auberge dont le patron, avant d'ouvrir la porte, demande à qui il a affaire. Le noble gentilhomme décline ses noms: Duque de Bejar, Marques de Gibraleon, Conde de Bañalcazar y Bañares, Visconde de la Puebla de Alcocer, Señor de las Villas de Capilla, Curiel y Burguillos. L'aubergiste, qui ignorait qu'un espagnol pouvait avoir six ou huit noms différents, réplique: Messieurs, vous êtes beaucoup trop nombreux, je ne puis vous loger; il laisse le seigneur dans la rue et se prive ainsi d'un hôte qui lui aurait valu un beau bénéfice. Une mésaventure un peu analogue est arrivée à un étudiant en médecine désireux d'apprendre la sémiologie des maladies du système nerveux. Parcourant la table des matières d'un livre qu'on lui avait recommandé, il trouve en particulier, pour ce qui concerne l'examen des membres inférieurs, l'indication des signes suivants: réflexes de défense, réflexe antagoniste de Schaefer, Unterschenkelphaenomen d'Oppenheim, réflexe fléchisseur dorso-plantaire de Bechterew, triple retrait du membre inférieur, phénomène des raccourcisseurs, réflexes d'automatisme médullaire, massreflex. Ne sachant pas que toutes ces dénominations se rapportaient, au moins en très grande partie, à un seul et même phénomène, et se jugeant incapable de loger dans son esprit tant de données qu'il croyait différentes, il renonça à cette étude et se priva ainsi d'une notion facile à acquérir et qui lui aurait été très utile.

Je ne veux pas soutenir que le sujet dont je me propose de vous entretenir soit en tous points définitivement fixé et ne comporte plus de discussion; vous verrez dans la suite qu'il n'en est pas ainsi; mais je

[1] A Lecture delivered at the Royal Society of Medicine, London, with presentation of cases and cinematograph films.

crois pouvoir dire que la question est fort simple en ce qui regarde la clinique, les moyens qu'il faut employer pour mettre en évidence les réflexes dont nous allons nous occuper et certaines conséquences que l'on peut en déduire pour le diagnostic.

Me plaçant d'abord sur le terrain de l'observation et écartant les interprétations pathogéniques, je vais décrire les phénomènes que j'ai en vue. Il s'agit de réactions motrices consécutives à des excitations cutanées ou à des excitations profondes. Pour commencer, j'envisagerai uniquement les réactions observées aux membres inférieurs du côté excité, faisant abstraction des orteils (c'est là une dissociation artificielle il est vrai, mais vous verrez ultérieurement pourquoi je la fais) et me bornant à observer les mouvements exécutés par le pied, la jambe et la cuisse. Voici en quoi consistent ces réactions: sous l'influence d'excitations du membre inférieur telles que le frottement de la plante du pied avec une épingle, le pincement de la peau de la région dorsale du pied ou de la jambe, notamment à sa partie inférieure, il se produit, outre une contraction du fascia lata, une flexion du pied sur la jambe, de la jambe sur la cuisse, de la cuisse sur le bassin ; l'attitude en flexion se maintient généralement un laps de temps appréciable et le membre inférieur ne reprend qu'avec une certaine lenteur son attitude primitive ; dans certains cas, la contraction musculaire dure dix, quinze secondes, davantage même, surtout si l'excitation qui a provoqué le mouvement est continue, et il est possible quelquefois de déterminer ainsi une sorte de contracture transitoire.

Ce mode de réaction (triple flexion) susceptible d'être obtenue par des excitations portant sur diverses parties du membre inférieur est un des plus communs et l'on a couramment l'occasion de l'observer en clinique. On le constate ordinairement chez des malades présentant des troubles notables de la motilité volontaire, et c'est là qu'il acquiert le maximum d'intensité, mais il peut être très net chez des sujets encore assez valides.

L'électrisation avec des courants voltaïques ou avec des courants faradiques, l'application d'un corps chaud ou d'un corps froid, la pression exercée sur les parties profondes, les tractions constituent aussi de bons procédés d'excitation. Bechterew, puis Pierre Marie et Foix, ont recommandé une manœuvre indiquée déjà par Charcot et qui consiste à fléchir fortement les orteils sur la plante, en même temps qu'on abaisse l'extrémité antérieure du pied.

La zone réflexogène est plus ou moins étendue suivant les malades. Souvent, elle occupe seulement le pied et la jambe et s'arrête approximativement au genou, mais parfois elle s'étend même à la cuisse et à une partie plus ou moins vaste du tronc ; nous reviendrons ultérieure-

ment sur ce point. Dans certains cas, tandis que l'excitation du pied et de la jambe donne lieu au movement habituel, c'est à dire à la triple flexion, une irritation portant sur la cuisse est suivie d'une extension des trois segments. Voici une autre modalité de la réaction dont je m'occupe : le pincement de la peau de la partie inférieure de la jambe est suivi d'une flexion du pied et d'une extension de la jambe sur la cuisse ; j'ai particulièrement observé cette modalité chez des malades plus ou moins contracturés, dont les jambes, qui d'habitude se maintenaient en extension, avaient été préalablement placées par moi en demi-flexion. Il m'est arrivé aussi de voir ceci : l'excitation, provoquant toujours une flexion du pied, accentuait un peu, pour commencer, l'attitude de la jambe en flexion, laquelle était immédiatement suivie d'un fort mouvement en sens inverse qui ramenait la jambe en extension. Parfois, quel que soit le sens du mouvement, flexion ou extension, on constate des contractions dans les muscles de groupes opposés, et l'on peut concevoir que le sens du mouvement soit conditionné en partie par la position où se trouvent au momeut de l'excitation les segments du membre les uns par rapport aux autres.

Il y a de grandes différences en ce qui concerne l'intensité des réflexes, l'amplitude des mouvements. Tantôt, le moindre attouchement de la peau d'un membre suffira à déclencher une flexion très prononcée de tous ses segments et amènera une série de mouvements alternatifs de flexion et d'extension ; tantôt, au contraire, le pincement très vif de la peau ne déterminera qu'avec peine une simple flexion du pied. Entre ces types extrêmes se placent tous les intermédiaires. En outre, il est à remarquer que si, pour chaque malade, il existe, au cours d'un examen, une certaine proportionalité entre l'intensité de l'excitation et celle de la réaction, le rapport entre ces deux éléments peut varier notablement lorsque l'on considère les résultats de deux examens pratiqués à quelques jours ou même à quelques heures d'intervalle.

La description qui précède se rapporte à des observations faites sur des sujets atteints d'affections organiques intéressant la voie pyramidale.

Mais, avant d'aller plus loin, je dois discuter les questions suivantes : les réactions signalées sont-elles toutes pathologiques ; quelques-unes d'entre elles peuvent-elles au contraire être obtenues à l'état physiologique ; y a-t-il des caractères permettant d'affirmer la nature pathologique de ces réactions ou de quelques-unes d'entre elles ?

Pour résoudre le problème, il est indispensable d'avoir examiné un grand nombre d'individus normaux et de savoir comment chez eux les membres inférieurs se comportent vis-à-vis d'excitations diverses. Or, voici ce qui paraît bien établi. Une excitation de la plante du pied telle que le frottement avec une épingle est souvent suivie, élimination faite

du mouvement des orteils sur lequel je reviendrai ultérieurement, d'une contraction du fascia lata que Brissaud a très bien décrite et d'une flexion du pied, de la jambe et de la cuisse. Ce sont là les mêmes mouvements que ceux qu'on observe à l'état pathologique. Mais chez le sujet normal la contraction est rapide, de courte durée, tandis que chez les malades dont il est question l'attitude en flexion obtenue par l'excitation plantaire se maintient généralement quelque temps et ne reprend que lentement sa position primitive, ainsi que je l'ai dit précédemment ; en outre chez ces derniers, l'amplitude du mouvement est bien plus marquée d'habitude. Ces différences sont souvent suffisantes pour établir une ligne de démarcation nette entre l'état physiologique et l'état pathologique. Toutefois, en se fondant uniquement sur ce qui vient d'être dit, des médecins encore peu expérimentés en clinique neurologique et n'ayant pas la vision précise de la forme des mouvements réflexes pathologiques seraient exposés à des erreurs ; ajoutons à cela que ces mouvements n'ont pas toujours la lenteur ci-dessus décrite.

Un autre caractère plus important et conduisant à distinguer l'état physiologique de l'état pathologique est le suivant : chez l'homme normal, l'excitation d'une région quelconque du membre, *hors de la plante du pied*, si elle peut provoquer un mouvement de flexion de la cuisse et de la jambe, ne donne jamais lieu à la flexion du pied. Je crois utile d'appuyer sur ce point. Sans doute, le retrait de la cuisse et celui de la jambe qu'on peut observer alors semblent volontaires et diffèrent d'habitude des réactions réflexes par les caractères du mouvement, ainsi que par ce fait que la contraction spéciale du tenseur du fascia lata signalée plus haut fait défaut ; mais, je le répète, sans autres moyens distinctifs, la confusion entre l'état physiologique et l'état pathologique pourrait être malaisée à éviter. Au contraire, l'absence pour ainsi dire constante de la flexion du pied chez le sujet normal (exception faite pour un cas de simulation qu'on pourrait d'ailleurs dépister) rend simple la solution du problème. *La flexion du pied obtenue par l'excitation d'une autre région que la plante du pied permet d'affirmer qu'on a affaire à un état morbide.*

Ce signe à lui seul me paraît donc décisif ; c'est le criterium de l'état pathologique. Il va sans dire que la conviction qu'il entraîne ne peut que se fortifier lorsque ce caractère s'associe au précédent, à la lenteur de la contraction et surtout de la décontraction. Au risque de décourager l'étudiant dont je vous parlais au début de cette Conférence, je propose une expression nouvelle : "*signe de la flexion réflexe du pied*" pour désigner les réflexes pathologiques que nous étudions. Le moyen le plus simple pour constater ce phénomène est de pincer la peau du dos du pied ou de la partie inférieure de la jambe. J'insiste auprès de ceux de mes auditeurs qui sont des débutants sur l'intérêt qu'il y a à connaître ce

signe, lequel a le double mérite d'être d'une exploration très facile et d'avoir une grande valeur clinique puisqu'il décèle l'existence d'une perturbation de la voie pyramidale, que celle-ci siège dans l'encéphale ou dans la moelle. S'ils retiennent seulement cette donnée, j'aurai la satisfaction de croire qu'ils n'ont pas perdu l'heure qu'ils ont bien voulu me consacrer.

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Le retrait du membre inférieur, et notamment la flexion du pied, a manifestement des rapports assez étroits avec le signe des orteils, puisque ces deux phénomènes paraissent bien caractéristiques d'une perturbation de la voie pyramidale ; ces deux réactions motrices se produisent généralement dans les mêmes conditions et suivant un mode semblable ; je viens de dire que dans la triple flexion la contraction et surtout la décontraction sont lentes ; or, dans mon travail sur le phénomène des orteils, en 1898, je faisais déjà remarquer que le plus souvent l'extension des orteils (réaction pathologique) est exécutée avec plus de lenteur que la flexion des orteils (réaction normale). Je suis très porté à admettre—j'y reviendrai plus loin—que la pathogénie du signe des orteils ressemble à celle de la triple flexion. Mais envisageant la question du point de vue clinique et, comme je l'ai dit dans mon travail sur les réflexes de défense publié en 1914, " mettant absolument de côté tout ce qui concerne l'interprétation physiopathologique de ces phénomènes," j'ai soutenu que les liens entre les réflexes dits de défense et le phénomène des orteils ne sont pas indissolubles, que par conséquent il y avait lieu de ne pas les fusionner complètement.

MM. Marie et Foix, tout en admettant qu'ils peuvent être dissociés et tout en reconnaissant que je n'ai pas prétendu qu'il y eût différence absolue de nature entre le signe des orteils et les réflexes cutanés de défense, déclarent être d'un avis contraire au mien. " Pour nous, au contraire," écrivent nos collègues, " le signe de Babinski appartient à l'ensemble des mouvements automatiques complexes dont le mécanisme est un mécanisme de marche."

M. Walshe, sans être d'accord avec les auteurs précédents sur le mécanisme de ces réactions motrices, ne veut établir aucune distinction entre ces deux phénomènes et il écrit que tandis que je regarde la triple flexion comme de nature défensive, je considère l' " extensor response " comme un réflexe distinct et séparé, une chose à part pour laquelle je n'offre pas d'explication et qui resterait pour moi un signe mystique et inexplicable d'affection du faisceau pyramidal. Je répondrai à cela que, si je n'ai pas cherché à expliquer le phénomène des orteils quand je l'ai

décrit, je n'ai jamais dit qu'il fût inexplicable, et je ne vois pas bien ce qu'il y a de mystique à se cantonner dans le domaine de l'observation clinique ; j'aurais plutôt mérité le reproche d'être " terre à terre."

Il est incontestable, je le répète, que l'extension réflexe des orteils et la flexion réflexe du pied sont, dans la majorité des cas, associées et je serais sans doute le dernier à le nier, ayant été le premier à signaler en 1900, à propos du travail de Schaefer sur le réflexe antagoniste du pied, dont je vous entretiendrai dans un instant, que, dans l'hémiplégie organique, le pincement de la peau en diverses parties du pied et de la jambe peut provoquer à la fois ces deux réactions. Mais, encore une fois, l'une peut se produire sans l'autre. On peut observer non seulement le phénomène des orteils en l'absence du signe de la flexion réflexe du pied mais aussi la disposition inverse.

J'ai cité autrefois, à l'appui de mon opinion, une Observation anatomo-clinique relatée par Dejerine, Lévi-Valensi et Long [14, 15] : il s'agissait d'un cas de paraplégie par section complète de la moelle où il existait, en même temps que des réflexes de défense très nets, une flexion plantaire des orteils des plus franches ; il est à remarquer qu'il n'y avait pas trace de réaction de dégénérescence dans les muscles de la jambe. M. Walshe récuse cette Observation à cause du passage suivant qu'on y trouve : " Les pieds sont en varus équin et les orteils en flexion. Cette déformation est aujourd'hui fixée par des rétractions fibro-musculaires." La critique de M. Walshe n'est pas sans valeur. Mais il y a tout lieu de penser que ces rétractions n'étaient pas assez marquées, au moins pendant un certain laps de temps, pour entraver l'exploration des réflexes, car M. Dejerine donne à cet égard des renseignements tellement circonstanciés qu'un doute ne peut guère subsister. Il écrit en effet : " J'arrive maintenant à une question encore plus importante peut-être que les précédentes, à savoir l'état du *réflexe cutané plantaire*. Pendant les six mois que passa ce malade dans mon service, le réflexe cutané de la plante du pied se faisait des deux côtés en flexion plantaire, c'est à dire comme à l'état physiologique."

Je rappelle aussi l'observation publiée par Pastine [27] se rapportant à un sujet atteint de paraplégie motrice absolue avec troubles très accentués de la sensibilité superficielle et profonde des membres inférieurs. J'extrais de ce travail le passage suivant : " Le fait intéressant pour la question qui nous occupe me semble être celui-ci : la possibilité presque constante d'obtenir, par une excitation plantaire un peu forte ou répétée, ou encore mieux par un pincement énergique de la peau du dos des pieds, le mouvement réflexe de flexion du pied, de la jambe et de la cuisse associé à la flexion nette de tous les orteils, et par une excitation minimale du bord plantaire externe, le signe de Babinski nettement

positif et isolé. Dans ce cas, c'est la flexion du gros orteil qui fait partie du mouvement général de retrait, et pourtant l'extension pathologique du même orteil existe dans toute sa pureté."

Du reste, déjà dans un travail publié par moi en mars 1899 [2], basé en particulier sur une observation qui est un type de paraplégie en flexion, avec mouvements spasmodiques intermittents accentuant la flexion des cuisses et des jambes, il est dit expressément que le réflexe cutané plantaire est normal.

Des expériences de M. Ozorio de Almeida, confirmées par moi, ont montré que chez des sujets présentant le signe des orteils, une compression du membre inférieur avec une bande élastique peut amener transitoirement la réapparition du mouvement réflexe de flexion des orteils ; or, le pied peut continuer alors à exécuter un mouvement réflexe en flexion à la suite de l'excitation de sa région dorsale.

MM. Marie et Foix, dans un article sur "les réflexes d'automatisme médullaire [22]," écrivent à ce sujet : "Nous avons, sur la plupart de ces points, pu reproduire les expériences de Babinski, mais l'interprétation que nous inclinons à donner nous apparaît comme très différente de la sienne" . . . . . "Il est aisé de se convaincre par l'observation attentive que l'application de la bande d'Esmarch agit en supprimant momentanément l'excitabilité réflexe des muscles ischémiés . . . . . ." Les muscles extenseurs, par suite des dispositions anatomiques, subiraient une ischémie plus intense que les fléchisseurs.

L'interprétation donnée par mes collègues me semble discutable. Elle ne permet guère de comprendre ce fait noté chez certains sujets et que je rappelle : avant la compression, réflexe plantaire toujours en extension quelle que soit la région de la plante que l'on excite ; après la compression, réflexe en extension ou en flexion suivant qu'on excite le bord externe ou le bord interne de la plante.

De plus, en variant la durée de la compression, j'ai fait plusieurs fois les constatations suivantes : après avoir enlevé la bande à un moment où le réflexe se faisait encore en extension, j'ai vu cependant, au bout de quelques instants, au retour de l'irrigation sanguine, le réflexe en flexion remplacer pour quelque temps le mouvement réflexe précédent. Il m'est arrivé alors d'observer, après avoir pincé la peau de la jambe ou du dos du pied, la flexion des orteils associée à une forte flexion du pied.

Ces faits ne sont guère en concordance avec l'interprétation proposée par MM. Marie et Foix. D'ailleurs, celle-ci serait-elle juste, elle n'infirmerait pas ma thèse, car me plaçant simplement sur le terrain de l'observation, et sans contester aucunement les relations qui unissent la flexion réflexe du pied avec l'extension des orteils, les connaissant

même depuis plus de vingt ans, comme je viens de le dire, j'ai voulu établir qu'il pouvait y avoir dissociation de ces deux phénomènes. Les cas où cette dissociation existe, sans être très communs, ne sont pas tout à fait exceptionnels ; j'en ai observé déja un assez grand nombre et vous aurez l'occasion de la constater vous-mêmes sur l'un des films que je ferai passer devant vos yeux. Il s'agit d'un malade atteint de paraplégie incomplète liée vraisemblablement à une plaque de sclérose ; d'un côté on observe la trépidation épileptoïde du pied et le triple retrait associé à l'extension du gros orteil ; de l'autre côté la trépidation épileptoïde et le triple retrait existent nettement, mais ce dernier phénomène coïncide avec un réflexe plantaire en flexion bien qu'il n'existe pas de réaction de dégénérescence dans les muscles de la jambe.

Avant de terminer ce chapitre, je ferai remarquer que Marie et Foix, malgré leur désaccord apparent avec moi, semblent avoir dans le fond une opinion analogue à la mienne, puisque dans leur premier article sur le retrait réflexe du membre inférieur [21] ils écrivent ceci : " Il (le retrait réflexe) est extrêmement fréquent dans l'hémiplégie constituée. Il est en général associé au signe de Babinski, mais ne lui est pas superposable. On l'observe en effet en dehors de ce signe, particulièrement chez certains pseudo-bulbaires, ou dans certains cas d'hémiplégie ancienne " ; et, dans un deuxième travail sur les réflexes d'automatisme médullaire [22], ils écrivent encore : " L'on peut cependant voir, dans les cas où, par suite du combat entre le réflexe normal en flexion et le réflexe pathologique en extension, le mouvement des orteils est nul ou même en flexion, le signe des raccourcisseurs établir une lésion que la recherche du signe de Babinski n'avait pu dépister."

N'est-ce pas absolument conforme à ce que j'ai soutenu ?

Il me semble intéressant, à l'appui de ma thèse, de noter que M. Van Woerkom, dans un travail " Sur la signification physiologique des réflexes cutanés des membres inférieurs " [33], écrit ceci : " Pourtant, le lien qui relie le signe de Babinski au ' flexion réflexe ' n'est pas indissoluble."

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Contrairement à l'usage suivant lequel l'exposé d'une question est généralement précédé de l'indication des noms de ceux qui s'en sont principalement occupés, j'ai cherché d'abord à faire une description des faits cliniques suffisante pour bien délimiter mon sujet. Je crois le moment venu de faire un historique, surtout étant donné que j'ai déjà été entraîné à signaler quelques controverses entre neurologistes.

Les phénomènes que nous étudions paraissent avoir été mentionnés

pour la première fois en 1784 par Prochaska. L'expérience faite par cet auteur a été maintes fois reproduite depuis ; Schiff, Vulpian, Brown-Séquard, pour ne citer que quelques-uns des physiologistes qui se sont occupés des réflexes de défense, ont vu comme Prochaska qu'une grenouille ou un mammifère dont on sectionne la moelle dorsale retire brusquement la patte en fléchissant les divers segments de ce membre les uns sur les autres quand on en pique l'extrémité.

Ce mouvement reproduit assez exactement celui qu'effectue, sous la même excitation, une grenouille dont la moelle est intacte et qui cherche à se dérober à l'injure extérieure, à se défendre. Le phénomène fut pour cela qualifié de " mouvement réflexe de défense," et l'usage a consacré cette dénomination.

Les physiologistes seuls s'occupèrent d'abord de ces mouvements particuliers. Vulpian, Brown-Séquard signalent il est vrai leur existence dans les tumeurs de la moelle et dans quelques autres affections de cette partie du névraxe, mais ils n'en indiquent pas la valeur sémiologique précise.

L'attention qu'on leur avait prêtée fut même bientôt très réduite lorsqu'on acquit la connaissance des réflexes tendineux et qu'on s'attacha à leur étude. La brièveté des mentions qu'on trouve au sujet des réflexes de défense dans les meilleurs traités classiques de neurologie fait foi, d'ailleurs, de ce réel discrédit.

C'est depuis vingt-cinq ans environ, et à la suite de ma communication sur le réflexe cutané plantaire et le phénomène des orteils, que l'attention a été de nouveau dirigée sur les réflexes de défense, bien qu'on se soit servi parfois d'autres termes pour désigner les faits qui s'y rapportaient.

Schaefer, dans un travail publié en novembre 1899 [31], décrit un phénomène réflexe dont voici les caractères : lorsqu'on presse énergiquement, entre le pouce et l'index, le tendon d'Achille dans son tiers moyen ou son tiers supérieur, on provoque chez l'individu sain une sensation de douleur légère et en même temps une très faible extension du pied et parfois aussi une flexion des orteils. Or, dans certains cas pathologiques, chez des malades atteints d'hémiplégie cérébrale organique, la même manœuvre donne lieu à une sensation de douleur plus intense et, en outre, à une flexion du pied ainsi qu'à une extension des orteils du côté paralysé. Ce réflexe pathologique se distinguerait des autres réflexes tendineux parceque la réaction, au lieu de s'opérer dans le muscle dont le tendon est excité, se manifesterait dans les antagonistes, d'où la dénomination de *réflexe antagoniste* que Schaefer propose de donner à ce phénomène.

Ainsi que je l'ai dit dans une communication à la Société de Neurologie

en janvier 1900, il est aisé de vérifier les faits décrits par Schaefer qui sont absolument exacts, mais ses déductions comportent des critiques : d'une part, l'extension des orteils qu'il indique n'est autre chose que le phénomène des orteils découvert antérieurement ; d'autre part, rien n'autorise à admettre que la réaction obtenue dans les expériences de Schaefer constitue un réflexe tendineux antagoniste. J'ai montré, en effet, que chez les hémiplégiques qui présentent ces réactions, extension des orteils et flexion du pied, celles-ci sont généralement obtenues par le pincement de la peau seule dans le voisinage du tendon ou encore en d'autres parties du membre inférieur. Comme on le voit, ces observations ont conduit à cette notion nouvelle, dont j'ai fait ressortir précédemment l'intérêt, qu'une excitation du membre inférieur, hors de la zone plantaire, incapable de produire une flexion réflexe du pied à l'état normal, peut en déterminer une dans l'hémiplégie organique, affection dans laquelle la voie pyramidale est intéressée.

Les réactions décrites ultérieurement par Oppenheim sous la dénomination d' " Unterschenkelphaenomen " dans les affections pyramidales sont identiques aux précédentes. Voici en quoi elles consistent : tandis que l'excitation des téguments de la partie interne de la jambe provoquée par le frottement ne détermine à l'état normal aucun réflexe, ou seulement une flexion des quatre petits orteils, cette excitation, dans les cas où il y a une lésion de la voie pyramidale, produit une contraction des muscles extenseur propre du gros orteil, jambier antérieur, extenseur commun des orteils et parfois des muscles péroniers.

Van Gehuchten [32], en août 1900, dans une étude " sur les réflexes cutanés et les réflexes tendineux," s'occupe particulièrement des réflexes de défense dans les lésions atteignant le système pyramidal ; il se sert de ces termes : " mouvement de retrait brusque de tout le membre : flexion du pied sur la jambe, de la jambe sur la cuisse, de la cuisse sur le bassin, avec mouvements d'adduction de la cuisse."

Je reviens sur ce sujet dans un travail publié en 1904 à la Société de Neurologie et intitulé : " Sur la transformation du régime des réflexes cutanés dans les affections du système pyramidal."

Bechterew [11] en 1906 a publié une note sur les mouvements réflexes produits par la manœuvre qui consiste à flechir le pied et les orteils.

En mai 1910, nous cherchons, Jarkowski et moi [7], à utiliser les réflexes de défense pour déterminer le niveau inférieur d'une lésion spinale.

En juillet 1910, Pierre Marie et Foix publient leur premier travail sur ce sujet [21]. Il est intitulé : " Sur le retrait du membre inférieur provoqué par la flexion forcée des orteils."

En 1910 Claude [13] traite de l'hyperkinésie réflexe qu'on peut observer au membre supérieur.

En janvier 1911 [3], je décris " la paraplégie spasmodique avec contracture en flexion et contractions musculaires involontaires " et je fais ressortir les liens qui l'unissent aux réflexes de défense. En mai 1912, je reviens sur ce sujet [4].

Nouveau travail de Marie et Foix en mai 1912 [22], intitulé : " Les réflexes d'automatisme médullaire et le phénomène des raccourcisseurs. Leur valeur sémiologique. Leur signification physiologique."

En 1912, mémoire de van Woerkom [33] : " Sur la signification physiologique des réflexes cutanés des membres inférieurs."

En 1914-1915 [6], je publie une étude sur les réflexes de défense, et quelques semaines plus tard Pierre Marie et Foix [23] font paraître à leur tour un mémoire sur " les réflexes d'automatisme médullaire dits de défense."

Dans un travail intitulé : " Quelques remarques sur les réflexes de défense dits d'automatisme médullaire " [18], Jarkowski discute la pathogénie de ces phénomènes.

Voici maintenant l'indication de plusieurs travaux sur le sujet qui nous occupe qui sont l'œuvre de neurologistes anglais :

F. M. R. Walshe : " The Physiological Significance of the Reflex Phenomena in Spastic Paralysis of the Lower Limbs " [34], et " On the Genesis and Physiological Significance of Spasticity and other Disorders of Motor Innervation " [35].

Henry Head and George Riddoch : " The Automatic Bladder, Excessive Sweating and some other Reflex Conditions in Gross Injuries of the Spinal Cord " [17].

George Riddoch : " The Reflex Functions of the Completely Divided Spinal Cord in Man " [28], et " The Clinical Picture of Complete Transverse Division of the Spinal Cord " [29].

George Riddoch and Farquhar Buzzard : " Reflex Movements and Postural Reactions in Quadriplegia and Hemiplegia, with especial reference to those of the Upper Limb " [30].

Je fais une place à part au grand physiologiste Sherrington dont les découvertes ont orienté les recherches des neurologistes anglais et les ont inspirés dans leurs interprétations des faits cliniques observés. Le nom de Philipson, collaborateur de Sherrington, mérite aussi d'être particulièrement retenu.

* * * *

Après ce court historique, reprenons le fil de nos idées. J'ai dit que si le lien entre les réflexes de défense pathologiques, notamment la flexion

réflexe du pied et le signe des orteils, n'est pas indissoluble, il est pourtant assez étroit.

Et quelles sont les relations entre ces diverses réactions et la surréflectivité tendineuse qui elle aussi constitue une signe de perturbation de la voie pyramidale? On peut dire, a priori, que ces deux ordres de phénomènes doivent être souvent associés, mais c'est une liaison beaucoup moindre que la précédente. Dans le tabes dorsal spasmodique avec surréflectivité tendineuse extrêmement forte, la flexion réflexe du pied est généralement faible ou même fait défaut, ce qui, à la vérité, pourrait tenir à la contracture en extension qui entrave la manifestation des réflexes de défense. Dans l'hémiplégie organique avec exagération notable des réflexes tendineux et trépidation épileptoïde, la flexion réflexe du pied peut aussi manquer de même qu'il y a parfois absence du signe des orteils.

Mais ce qui est plus frappant c'est la disposition inverse: affaiblissement ou abolition des réflexes tendineux avec exagération notable des réflexes de défense. C'est ce qu'on observe d'habitude dans la maladie de Friedreich; c'est ce qu'on peut voir dans le tabes associé à une lésion pyramidale. J'ai insisté déjà en 1898, dans un travail relatif au phénomène des orteils [1], sur la coexistence de ce signe avec la subréflectivité ou l'irréflectivité tendineuse. "J'ai constaté, disais-je, ce phénomène dans plusieurs cas d'hémiplégie récente flasque, où les réflexes tendineux étaient normaux, affaiblis ou même abolis du côté paralysé."

On observe très couramment des malades atteints de paraplégie crurale plus ou moins marquée avec réflexes tendineux normaux, sans trace de trépidation épileptoïde du pied et avec réflexes de défense très caractérisés. Je suis convaincu, certain même, qu'autrefois beaucoup de malades de ce genre ont été considérés comme atteints de paraplégie hystérique. Ces erreurs sont devenues bien plus rares depuis que la connaissance des signes en question s'est répandue parmi les praticiens.

Dans la paraplégie en flexion, sur laquelle je reviendrai plus loin et dont le trait le plus essentiel est l'exagération des réflexes de défense, les réflexes tendineux peuvent aussi être exagérés, mais il n'en est pas toujours ainsi: ils sont parfois d'une intensité moyenne, ils peuvent être faibles et semblent même abolis dans certains cas. Je sais bien que l'exploration des réflexes tendineux est rendue quelquefois difficile par les rétractions fibro-tendineuses, par l'intensité et la fréquence des spasmes qui se produisent; mais en renouvelant les explorations à plusieurs reprises, en saisissant, pour les pratiquer, les moments où le spasme cesse, il est ordinairement possible de se rendre compte de l'état de la réflectivité tendineuse. Si j'ai bien compris ce qu'a écrit M. Walshe

à ce sujet, il est d'avis que dans la paraplégie en flexion, si les réflexes tendineux des extenseurs peuvent être abolis, ceux des fléchisseurs sont toujours exagérés. Je ne puis souscrire à cette opinion, m'étant assuré dans quelques cas de paraplégie en flexion que les réflexes tendineux des fléchisseurs de la jambe sur la cuisse n'étaient pas du tout au-dessus de la normale et paraissaient même plutôt faibles.

Dans la paraplégie en flexion, l'affaiblissement des réflexes tendineux peut survenir après une période plus ou moins longue pendant laquelle il y a eu surréflectivité tendineuse. Mais il y a des cas où, dès le début, les réflexes tendineux sont amoindris. J'ai rapporté une Observation de ce genre; voici un passage du travail où ce fait est relaté [4] : " Ce qui est capital c'est que, chez cette malade, où l'existence d'une affection organique de la moelle intéressant les faisceaux pyramidaux est incontestable, on observe une contracture associée à une abolition à peu près complète des réflexes tendineux et à des réflexes de défense extrêmement forts. Ce fait constitue un nouveau document relatif à l'histoire de la *paraplégie spasmodique organique avec contracture en flexion et contractions musculaires involontaires*, et il mérite pour plusieurs motifs d'attirer l'attention.

" Tandis que, chez les sujets où la contracture en flexion est permanente et a acquis une grande intensité, la faiblesse ou l'abolition des réflexes tendineux est difficile à apprécier et ne peut être affirmée qu' après des examens plusieurs fois renouvelés; dans le cas particulier, la contracture en flexion étant intermittente, on est à même, pendant les phases de détente qui sont très fréquentes, de se rendre un compte exact des réflexes tendineux; on s'assure aisément que le réflexe rotulien droit et les réflexes achilléens sont abolis. J'ajoute que l'affaiblissement des réflexes tendineux a été noté, dans ce cas, dès le début de l'affection et n'a pas été précédé de l'exagération de ces réflexes, ainsi que cela se voit assez souvent dans cette forme de paraplégie."

* * * *

L'exagération des réflexes de défense conduit-elle seulement au diagnostic de perturbation de la voie pyramidale? N'est-elle pas en mesure de fournir d'autres renseignements ayant une portée pratique, notamment dans les cas de compression de la moelle? C'est une question que nous avons cherché à résoudre, Jarkowski et moi. Mais il est de mon devoir de signaler un passage relatif à ce sujet que j'extrais de l'ouvrage de Duchenne de Boulogne " De l'électrisation localisée " et qui nous avait échappé autrefois : " Le point où le chatouillement de la peau cesse de provoquer des contractions réflexes indique

le niveau où existe la compression de la moelle." Il est à noter que ce moyen de localisation n'avait jamais été utilisé jusqu'à nous par aucun des neurologistes qui s'étaient occupés de repérer les tumeurs comprimant la moelle en vue de l'intervention chirurgicale. Voici, en résumé, ce que nous avons cru pouvoir déduire de nos investigations : Dans tout le territoire cutané en rapport avec la portion de la moelle sous-jacente à la partie inférieure de la lésion et dans ce territoire seulement, du moins quand la paraplégie est très marquée, une excitation peut provoquer des réflexes de défense. On possède ainsi un moyen de déterminer la limite inférieure de la compression. Ce n'est pas là une vue théorique. Cette donnée est établie déjà sur un certain nombre d'observations où le diagnostic a été vérifié pendant l'opération.

On a aussi publié, il est vrai, quelques faits qui tendent à infirmer cette notion, mais la contradiction n'est peut-être qu'apparente et j'ai cherché à l'expliquer dans mon travail de 1914, dont j'extrais le passage suivant :

" Cela tient, je pense, aux difficultés nombreuses que l'on rencontre quand on s'efforce de délimiter le territoire des réflexes de défense. On est exposé à des erreurs d'observation et d'interprétation sur lesquelles je crois devoir insister.

" C'est ainsi que chez des malades ayant conservé en partie leur motilité volitionnelle, un mouvement volontaire pourrait faire prendre le change et être considéré à tort pour un réflexe de défense. Chez d'autres malades, un mouvement spasmodique ' spontané ' risque d'être attribué à une excitation provoquée par l'expérimentateur, s'il coïncide avec cette dernière. On saisit immédiatement la portée d'une telle confusion, si cette excitation a été appliquée au-dessus du territoire des réflexes de défense.

" D'autre part, la réflectivité peut varier au cours d'un même examen et, a fortiori, d'un jour à l'autre ; on obtient ainsi des résultats en apparence contradictoires. De plus, la surréflectivité, que nous avons en vue, n'atteint son niveau maximum qu'à une période plus ou moins tardive de l'évolution de la maladie.

" Il faut donc renouveler les explorations pendant plusieurs jours, au besoin pendant plusieurs semaines, et retenir, entre les limites variées qui ont été obtenues, celle qui est la plus élevée, qu'elle se trouve des deux côtés au même niveau ou à des hauteurs différentes, pourvu qu'elle soit dûment établie.

" Il est encore essentiel de savoir que les réflexes de défense se laissent provoquer beaucoup plus facilement sur les membres inférieurs que sur le tronc et que parfois le domaine de la surréflectivité ne dépasse pas le pli de l'aine, même lorsque la limite inférieure de la lésion siège à la

partie moyenne de la moelle dorsale ou au-dessus. Notre expérience nous a appris qu'il fallait seulement tenir compte des cas où la surréflectivité envahit une partie plus ou moins étendue du tronc, à moins que d'autres symptômes ne permettent déjà de localiser la lésion dans la région lombaire ou sacrée.

" Enfin, je rappelle que les réflexes de défense se laissent provoquer de préférence tantôt par le pincement, tantôt par le froid, la chaleur, l'électricité ou la piqûre. Dans chaque cas particulier, il faut employer le mode d'excitation qui constitue le réactif le plus sensible.

" On voit, par ce qui précède, combien ces recherches sont délicates, et je conviens qu'un observateur, quelque averti et méthodique qu'il soit, ne parviendra pas toujours à obtenir de ses investigations sur les réflexes de défense des renseignements utilisables."

Il n'en est pas moins vrai, pensons-nous, que dans certains cas de compression spinale il sera possible d'acquérir ainsi des données intéressantes pour le diagnostic topographique des lésions, surtout si on les rapproche de celles, plus importantes sans aucun doute, qui sont fournies par les troubles de la sensibilité.

* * * *

Autre problème. L'intensité des réflexes de défense et les diversités de forme qu'ils présentent sont-elles en rapport avec l'intensité des lésions, le niveau où elles siègent et leur nature ? Dans mon article de 1898 j'écrivais déjà ceci à propos du signe des orteils : " Il faut donc bien remarquer que ce signe, s'il révèle l'existence d'une perturbation dans le système pyramidal, n'en dénote pas la gravité. . . . . Il semble même qu'il puisse parfois constituer le seul indice de cette perturbation." Je reviendrai dans un instant sur ce point.

Pour ce qui est relatif au niveau, j'ai dit autrefois et tous les neurologistes semblent d'accord là-dessus, que les réflexes de défense sont, d'une manière générale et sauf à la période initiale quand il y a shock, plus accentués dans les lésions spinales que dans les lésions cérébrales, ce qui tient peut-être en partie à ce que d'ordinaire les premières sont bilatérales, les secondes unilatérales.

En ce qui regarde la nature des lésions, d'après ce que j'ai observé, je pense que l'exagération des réflexes de défense est particulièrement intense et durable dans les cas de paraplégie spasmodique par compression de la moelle ou par sclérose spinale dans lesquels les altérations dégénératives du faisceau pyramidal font défaut ou sont peu prononcées. Plusieurs observations tendant à confirmer cette opinion ont été rapportées par divers auteurs [26].

Les faits de section complète de la moelle observés à la suite de traumatismes de guerre ont montré à MM. Head, Riddoch, à M Lhermitte que ces lésions, qui produisent le maximum de dégénération peuvent aussi se manifester, à une certaine période de leur évolution, par des réflexes de défense très marqués. Mais dans ces derniers cas, la phase pendant laquelle les réflexes de défense sont exagérés est relativement courte et la contracture qui se lie à ces réflexes dans la paraplégie que j'ai envisagée et dont nous aurons à nous occuper dans la suite, manque ou est peu marquée. En tout cas, mes observations ont montré que l'intensité des réflexes de défense n'est pas, tant s'en faut, en proportion directe avec le degré d'intensité de la dégénération secondaire. M. Walshe, à ce propos, dit ceci : Le point soulevé par Babinski qu'il peut n'y avoir que peu ou pas de dégénération secondaire de la voie pyramidale à l'examen anatomique dans de tels cas n'a pas de signification spéciale parceque, comme Gordon Holmes l'a montré, il n'y a pas de relation directe, constante entre la gravité des manifestations cliniques et la dégénération descendante secondaire. Une lésion en foyer de la moelle, dit-il, peut causer une paralysie spastique extrême et perte du contrôle sphinctérien, et cependant, à l'autopsie, il peut ne pas y avoir de dégénération spinale descendante.

Je sais cela depuis longtemps et j'ai précisément rapporté moi-même en 1899 une Observation de ce genre que j'ai déjà rappelée. Mais il faut savoir aussi qu'une paralysie complète due à une compression de la moelle, accompagnée de réflexes de défense très intenses, peut guérir totalement ; et cette régression des accidents n'est-elle pas expliquable par l'absence de dégénération ? C'est ce que j'ai cherché à mettre en lumière.

Je le répète, la présence de réflexes de défense même très prononcés et avec accompagnement de troubles moteurs des plus marqués, n'est pas nécessairement l'expression d'un état incurable. Entre autres faits à l'appui de cette notion, je puis vous citer quelques extraits d'une Observation publiée par Jarkowski, Lecène et moi [10] et intitulée : "Paraplégie crurale par néoplasme extra-dure-mérien. Opération. Guérison." En décembre 1911, on note ceci : "La malade présente une paraplégie spasmodique en extension avec troubles de la sensibilité remontant jusqu'à la ligne mamelonnaire. La paralysie des membres inférieurs est complète et ne cède même pas sous l'influence de divers procédés dynamogénisants (faradisation, application de la bande d'Esmarch). Cette contracture ne peut être vaincue que par un très grand effort ; pourtant, elle n'est pas toujours égale à elle-même et peut être diminuée par des mouvements passifs. De plus, la contracture en extension est entrecoupée de temps à autre par des mouvements spasmodiques invo-

lontaires qui déplacent brusquement les membres inférieurs, fléchissent la cuisse, la jambe et le pied, les allongent ensuite avec une grande force, en détachant le membre du plan du lit, et ainsi de suite, jusqu'à ce que le membre retrouve sa position primitive de repos.

" Ces spasmes se produisent soit dans un seul des membres inférieurs, soit dans les deux, et alors tantôt ils revêtent la même forme des deux côtés, tantôt ils donnent lieu à une flexion à droite et une extension à gauche ou vice-versa. Les réflexes tendineux des membres inférieurs sont nettement exagérés ; il y a de la trépidation épileptoïde du pied des deux côtés.

" On constate le signe des orteils des deux côtés.

" Les réflexes de défense sont fortement exagérés et peuvent être provoqués même par des excitations très légères. Leur forme varie suivant la position des membres et l'endroit de l'excitation, mais elle est sensiblement pareille à celle des spasmes involontaires spontanés."

La malade est opérée en janvier, 1912. L'intervention est suivie d'une amélioration qui se poursuit ensuite, mais lentement.

En juin 1914, on note : " Elle marche toute seule, sans canne, pas très vite, il est vrai, mais d'une manière à peu près normale ; elle ne traîne pas ses jambes ; elle ne fauche pas ; la pointe du pied ne butte pas contre le sol.

" Un examen objectif minutieux ne décèle comme reliquat des troubles d'autrefois qu'une tendance à l'extension des orteils et une légère exagération des réflexes de défense."

J'apprends ultérieurement que la guérison est devenue complète.

Ce n'est pas dans la patrie de l'illustre Horsley dont je m'honore d'avoir été l'ami, que je provoquerai de la surprise en rapportant l'observation d'une paraplégie due à une tumeur comprimant la moelle et guérie à la suite d'une intervention chirurgicale. Si je l'ai relatée, c'est afin de bien mettre en évidence ce fait que la surréflectivité défensive n'implique pas l'idée d'incurabilité.

Les réflexes de défense, après disparition complète des troubles moteurs, peuvent redevenir absolument normaux.

On a pris l'habitude de dire que l'exagération des réflexes de défense témoigne que la moelle est délivrée du joug des centres supérieurs ; mais, comme on le voit par ce qui précède, la moelle, en recouvrant les réflexes de défense de ses ancêtres, n'a pas reconquis toute leur indépendance ; pareille aux affranchis de Rome, elle ne jouit parfois que d'une liberté transitoire et elle est exposée à reprendre ses chaînes, ce qu'atteste le retour des réflexes à l'état physiologique.

Mais il y a plus : dans certains cas, les réflexes de défense pathologiques survivent à tous les autres troubles.

Entre autre malades de ce genre, j'en puis citer un qui, guéri d'une paraplégie par lésion syphilitique de la moelle, avait recouvré la motilité au point de pouvoir parcourir sans arrêt une distance de plus de dix kilomètres et qui cependant présentait d'une manière très nette le signe des orteils et le signe de la flexion réflexe du pied.

On peut dire qu'en pareille occurrence il s'agit de la part de la moelle d'une fanfaronnade, d'un bluff : elle affiche des airs d'indépendance, se prétend libérée, tout en obéissant servilement à l'encéphale, son maître.

Si la diminution progressive des réflexes de défense préalablement exagérés peut être un signe favorable, comme dans l'observation de tumeur que je viens de rapporter, elle peut au contraire dénoter une aggravation : dans les cas de section complète de la moelle, ces réflexes s'affaiblissent d'habitude à la période qui précède la mort.

J'ai été amené à vous indiquer l'état des réflexes de défense dans les sections spinales totales à la phase terminale, à la phase moyenne. Je dois vous exposer l'état de ces réflexes à la première phase, après le traumatisme. Sous l'influence du shock, les réflexes cutanés aux membres inférieurs peuvent être complètement abolis comme le sont les réflexes tendineux. Pour ce qui concerne les réflexes tendineux, dont je ne vous parle qu'incidemment, et contrairement à l'opinion émise par Bastian et acceptée pendant trente ans par la majorité des neurologistes, leur abolition n'est pas non plus définitive ; ils peuvent reparaître et même atteindre un degré plus élevé que la normale, mais leur retour est plus tardif que celui des réflexes cutanés. Au sujet de ces derniers, les opinions ne sont pas toutes concordantes, ce qui tient sans doute à la diversité des cas et à ce qu'un même auteur a eu seulement l'occasion d'observer un nombre de faits restreint. Il y aurait tantôt abolition du réflexe cutané plantaire, tantôt extension, tantôt flexion des orteils. D'après Guillain et Barré, le réflexe en flexion de ces paraplégiques se différencie de celui de l'homme sain par sa lenteur, son temps de latence prolongé, la persistance relative de l'attitude en flexion. Dans cette première phase, la zone réflexogène serait limitée, comme à l'état physiologique, à la zone plantaire, et ce n'est qu'ultérieurement qu'elle s'étendrait à tout le pied et à la jambe ; les réflexes deviennent de plus en plus forts et une exagération parfois très marquée des réflexes de défense se constitue alors.

Il y a lieu de comparer ces faits de paraplégie à début brusque avec les cas d'hémiplégie cérébrale succédant à un ictus apoplectique. Souvent, dès les premiers jours, alors que le malade est encore dans le coma, que la paralysie est complète et la surréflectivité tendineuse d'habitude affaiblie, on peut constater l'extension réflexe des orteils et la flexion

réflexe du pied. Dans quelques cas, des neurologistes, présents à une attaque, ont eu l'occasion de constater ces signes dès la première minute. L'exagération des réflexes de défense paraît donc bien plus précoce dans l'hémiplégie cérébrale vulgaire que dans la paraplégie spinale à début brusque, ce qui dépend peut-être de ce que le shock subi par la moelle est plus grand quand il s'agit d'une lésion bilatérale que lorsqu'on a affaire à une lésion unilatérale. C'est une disposition contraire de celle qu'on observe à une période plus avancée des lésions cérébrales et spinales, ainsi que nous l'avons dit précédemment. Dans les affections spinales occupant un seul côté, la réflectivité se comporte peut-être comme dans l'hémiplégie cérébrale. J'ai rapporté un cas d'hémiplégie spinale avec anesthésie croisée due à une hémisection traumatique de la moelle, à la partie moyenne de la région dorsale, et dans lequel, quinze heures après l'accident, le côté paralysé présentait de la flaccidité, de l'irréflectivité tendineuse en même temps que le phénomène des orteils.

Je dois poursuivre l'étude des sections spinales dans leurs relations avec les réflexes cutanés, les réflexes de défense, me rapportant surtout aux travaux de MM. Head et Riddoch qui ont cherché à établir le parti qu'on pourrait tirer de l'état des réflexes de défense au point de vue du diagnostic différentiel entre les sections complètes et les sections incomplètes de la moelle. Je me permettrai toutefois de soumettre à la critique quelques-unes des idées que ces auteurs ont énoncées.

Auparavant, je dois compléter ce que j'ai dit sur les réactions obtenues par l'excitation du membre inférieur, m'étant borné d'abord, afin de ne pas compliquer mon sujet, à décrire celles qui se produisent dans le membre excité. Or, l'excitation d'un des membres inférieurs peut déterminer aussi des mouvements réflexes dans l'autre membre, que j'ai seulement notés d'une manière incidente jusqu'à présent. Je ne puis mieux faire pour vous en donner une idée que de citer un passage du travail de MM. Marie et Foix [22]. Les observations qu'ils ont faites servent de base à leur conception du mécanisme de ce qu'ils appellent " les réflexes d'automatisme médullaire."

" Nous allons voir maintenant, écrivent-ils, qu'il peut exister chez l'homme, dans quelques cas seulement il est vrai, un *réflexe d'extension croisée* analogue au " crossed extension reflex " de Philipson.

" Pour l'observer, il faut choisir un malade très spasmodique, non pas, comme nous l'avons dit, un malade atteint de paraplégie spasmodique syphilitique, mais d'une paraplégie par compression, telle que celle du mal de Pott. Nous l'avons rencontrée, en outre, de la façon la plus indiscutable, au cours de la sclérose en plaques à forme spasmodique et de la syringomyélie.

"Voici comment il faut procéder chez l'homme: on place tout d'abord les membres inférieurs en flexion légère, puis par la flexion forcée des orteils on provoque d'un seul côté le phénomène des raccourcisseurs. L'excitation doit, pour déterminer le réflexe croisé, être forte, progressive et prolongée; aussi est-il préférable de choisir des malades présentant des troubles de la sensibilité, de manière à éviter les phénomènes douloureux.

"Dans ces conditions, on voit se produire en un premier temps la flexion du membre excité, puis, l'excitation persistant toujours, se produit en un deuxième temps qui suit plus ou moins vite le premier, se confondant souvent partiellement avec lui, l'extension du membre croisé. L'ensemble reproduit, on le voit, de la façon la plus typique le 'crossed extension reflex' de Philipson."

Nous sommes maintenant en mesure d'indiquer les caractères empruntés à l'état des réflexes de défense et qui permettent, d'après Head et Riddoch, d'affirmer que la section de la moelle est soit incomplète, soit complète.

Voici les caractères qui dénoteraient une *section incomplète :*

(*a*) Présence du "crossed reflex."

Dans les sections totales, il n'y aurait pas de véritables réflexes croisés ; dans six cas sur les huit cas observés, la flexion réflexe du côté excité s'associe à une flexion du côté opposé; on peut bien observer parfois de ce côté une contraction du quadriceps et des muscles du mollet, mais sans déplacement du membre.

La proposition de Riddoch constitute non une loi, mais une règle souffrant des exceptions si l'on s'en réfère à une Observation de Lhermitte [19] et dont voici le résumé: "Syndrome de section totale de la moelle dorsale moyenne. Phase de shock durant un mois et demi. Réapparition des réflexes tendineux ; extension du gros orteil ; mouvements automatiques spontanés extrêmement intenses, mouvements de défense très vifs, mictions réflexes et spontanées, érections fréquentes ; hypersudation dans le segment inférieur du corps." Or, à la page 62, on lit ceci : "Le blessé étant dans le decubitus latéral gauche on excite la face postérieure de la cuisse droite : le membre inférieur droit se fléchit, le gros orteil s'étend ; du côté opposé le membre inférieur s'allonge, le pied s'étend et les orteils se fléchissent (Réflexes d'extension croisée)."

(*b*) Présence des réflexes en extension, qui ne s'observeraient que quand il y a persistance de l'influence des centres supérieurs. Dans la section complète, l'extension se produirait exclusivement par relâchement des fléchisseurs.

Un passage de l'Observation précédente de Lhermitte semble montrer

qu'il n'en est pas toujours ainsi. A la page 63, où il est fait mention de l'état des reflexes cinquante-deux jours après l'examen précédent, nous trouvons ceci : " Les mouvements de défense sont toujours très accusés. Le pincement de la peau de la face antérieure de la cuisse détermine l'extension de la jambe et la contraction tonique du quadriceps ; quelquefois, le mouvement s'étend au membre opposé."

(*c*) Présence de ce que les auteurs anglais appellent " local sign " et qui consiste en ce que les réactions seraient différentes suivant les points excités. Si, par exemple, l'excitation de la plante du pied, selon qu'elle porte sur sa partie externe ou sa partie interne, provoque, outre la triple flexion, une abduction ou une adduction du pied, on pourrait affirmer que la section est incomplète.

D'après Riddoch, si je l'ai bien compris, dans la section incomplète, la zone réflexogène du réflexe en flexion ne dépasserait pas le genou. Cette opinion me semble en contradiction avec certains faits. Vous verrez sur un des films une malade atteinte de paraplégie incomplète ; elle peut mouvoir volontairement ses membres inférieurs et cependant l'excitation de l'abdomen avec un tube de glace provoque une flexion comme l'excitation du pied.

Par contre, on pourrait considérer, d'après MM. Head et Riddoch, comme caractéristique d'une *section totale*, d'une libération complète de la moelle, ce qu'ils appellent " Massreflex," c'est à dire réflexes, de défense toujours en flexion avec mictions réflexes et forte sudation dans le segment inférieur du corps.

J'ai eu l'occasion de décrire moi-même les troubles vésicaux en question dans mon travail déjà cité. Voici le passage qui s'y rapporte :

" Les grands mouvements des membres, qui s'imposent surtout à l'attention, furent seuls étudiés au début, mais un examen minutieux montre que d'autres groupes musculaires peuvent entrer en jeu, comme cela résulte des recherches faites par mon élève Barré. La contraction des muscles de la paroi abdominale provoque un retrait de l'abdomen ; celles des muscles de la paroi thoracique produit des spasmes respiratoires brusques. Ces divers mouvements se font généralement en même temps que ceux des membres ou les suivent à très court intervalle. Enfin, les muscles profonds du tronc, ceux qui sont en partie volontaires, comme le diaphragme, ou ceux qui sont spécialement adaptés à la vie végétative, comme les muscles intestinaux et les muscles vésicaux, peuvent également entrer en contraction en même temps que les muscles des membres ; les malades ont parfois alors des débâcles gazeuses ou des mictions involontaires qui témoignent de la mise en activité de certains de leurs muscles lisses."

Y a-t-il là des éléments de différenciation ?

Ce que je puis dire c'est que nous avons suivi très longtemps, Jarkowski et moi, un sujet atteint d'une paraplégie liée à des lésions spécifiques, paraplégie très grave, mais dans laquelle les mouvements volontaires n'étaient pas complètement abolis ; la moelle n'était donc pas entièrement libérée des centres supérieurs ; or, chez ce malade, bien souvent, des excitations diverses déterminaient, en même temps que des réflexes de défense, des mictions involontaires et l'évacuation de matières fécales.

Avant de terminer ce chapitre je ferai remarquer que l'on a très rarement l'occasion d'observer des cas avérés de section totale. Ce sont les blessures de guerre qui ont fourni le matériel d'études. Sans elle, la prétendue loi de Bastian ne serait pas encore abrogée. Mais avouez que les acquisitions neurologiques nouvelles sont une bien faible compensation des misères déchaînées par la catastrophe mondiale.

* * * *

Quelques mots sur les mouvements réflexes des membres supérieurs.

Claude, dans un travail : " Sur certains phénomènes d'hyperkinésie réflexe " [13] a décrit dans l'hémiplégie cérébrale des réactions motrices réflexes et a eu surtout en vue celles du membre supérieur.

J'ai mentionné des reflexes de défense du membre supérieur dans mon article de 1915 : " Ils consistent également, disais-je, en mouvements de retrait ou d'allongement, souvent combinés à de la pronation de l'avant-bras et de l'adduction du bras. Ces mouvements peuvent présenter des modalités diverses comme les réflexes du membre inférieur, mais ils sont plus souvent que ceux-ci localisés à un seul côté."

MM. George Riddoch et Farquhar Buzzard [30] ont fait une étude approfondie de ces réactions motrices dans un travail dont j'ai donné déjà l'indication bibliographique et sur lequel le manque de temps m'empêche d'insister.

* * * *

Comment se comportent les réflexes de défense pendant le sommeil artificiel ? Cela dépend sans doute de l'agent anesthésiant dont on fait usage. On sait que l'éther agit autrement sur les réflexes tendineux que le chloroforme. Je ne puis entrer dans les détails de cette question ; je me contenterai de livrer comme document l'Observation suivante recueillie avec un soin minutieux :

Compression de la moelle de D^5 à D^6 (il s'agit du sujet que vous verrez sur un de mes films et chez lequel le niveau inférieur de la compression correspondait à la limite supérieure des réflexes de défense) : Paraplégie incomplète avec contracture en extension

d'intensité moyenne. Hypoesthésie jusqu'à D^5. Réflexes rotuliens forts, trépidation épileptoïde du pied. Signe des orteils et flexion réflexe du pied très caractérisés. La malade reçoit une heure avant l'opération, en injection sous-cutanée, un centigramme de chlorhydrate de morphine et un milligramme de bromhydrate de scopolamine. Elle est ensuite endormie à l'éther avec l'appareil d'Ombredanne. L'état des réflexes tendineux et des réflexes de défense reste semblable à ce qu'il était précédemment à un moment où l'anesthésie, semblant complète, se traduit par l'abolition du réflexe cornéen, l'abolition presque complète des réflexes pupillaires, l'insensibilité au pincement avec une pince et à l'incision pratiquée pour l'intervention. Pendant vingt minutes, jusqu'au moment de l'ouverture du canal rachidien, la malade étant plongée dans un sommeil profond, les réflexes tendineux et les réflexes cutanés, examinés de deux minutes en deux minutes, ne subissent pas de modification appréciable. Je note seulement que la flexion réflexe du pied obtenue par le pincement de la peau de la jambe est particulièrement lente : le pied, après s'être fléchi, ne revient à sa position de départ qu'au bout de six à dix secondes. La contracture s'atténue progressivement.

Peu de temps après l'ouverture du canal rachidien et excision d'un tissu néoplasique un peu adhérent à la dure-mère, un nouvel examen des réflexes est fait, quatre ou cinq minutes après le précédent. Cette fois, transformation complète : tous les réflexes sont abolis. La pression artérielle qui avait été prise plusieurs fois depuis le début de l'opération et qu'on explore de nouveau à ce moment ne s'est pas modifiée : (16 avec la méthode des oscillations). Mais très peu de temps après, la pression systolique, recherchée de nouveau, n'est plus que de 5. A noter que la température rectale mesurée à ce moment est de 38°2 alors qu'elle était de 37°4 au début. Quant à la rigidité musculaire, elle a complètement disparu. En présence de cet état de shock, on met fin à l'opération. Une heure après, les réflexes rotuliens ont reparu, mais ils sont faibles ; les réflexes achilléens restent abolis ; le pincement de la peau de la face dorsale du pied ne provoque aucun mouvement ; l'excitation de la plante du pied détermine une forte extension du gros orteil, la triple flexion du pied, de la jambe et de la cuisse, et une contraction du tenseur du fascia lata. Le lendemain de l'opération le pincement du dos du pied déterminait l'extension des orteils et la flexion réflexe du pied.

* * *

Je vais actuellement étudier les réflexes de défense dans leurs rapports avec les troubles moteurs, la paraplégie spasmodique, la contracture.

Mes observations m'ont conduit à assigner à chacune de ces deux formes de paraplégie, celle en extension et celle en flexion, des caractères cliniques distinctifs, au milieu desquels les réflexes de défense occupent une place importante. Pour donner un aperçu exact des idées que j'ai exposées sur ce sujet, je pense que le mieux est d'extraire d'un travail que j'ai publié en 1912 [5], sur les réflexes tendineux et les réflexes osseux, les passages suivants :

"Je dois m'occuper, en y insistant, d'une variété de contracture sur laquelle j'ai appelé l'attention et qui, étant donné le but que nous visons, mérite d'être décrite. On l'observe surtout aux membres inférieurs et elle est un des éléments constitutifs d'une espèce de paraplégie dont on saisira mieux l'aspect en la rapprochant de la paraplégie spastique d'Erb. Celle-ci, nous le rappelons, se caractérise par les phénomènes suivants : (*a*) rigidité musculaire en extension, stable ; (*b*) simple parésie, c'est à dire affaiblissement peu prononcé de la motricité volontaire ; (*c*) exagération notable des réflexes tendineux avec trépidation épileptoïde du pied, et parfois danse de la rotule ; (*d*) réflexes de défense légèrement exagérés ou à peu près normaux ; (*e*) signe des orteils.

"Voici maintenant les caractères de la paraplégie que nous avons en vue : (*a*) rigidité musculaire en flexion, qui au début cesse par moments d'une manière complète ou presque complète, mais qui plus tard devient stable ; cependant cette stabilité n'atteint guère le même degré que dans la forme précédente ; elle est sujette à des variations fréquentes qui résultent des contractions involontaires des muscles des membres inférieurs ; ces contractions sont habituellement lentes ; elles donnent lieu à des mouvements alternatifs de flexion et d'extension avec prédominance d'action des fléchisseurs ; (*b*) motricité volontaire profondément troublée ; il peut y avoir paralysie complète ; (*c*) réflexes tendineux parfois exagérés, mais pouvant être normaux, affaiblis ou même abolis ; (*d*) réflexes de défense toujours très forts ; (*e*) dans la grande majorité des cas, signe des orteils. Ajoutons que la rigidité en flexion, quand elle est devenue stable, se complique presque inévitablement de rétractions fibro-tendineuses.

"Je ne m'étendrai pas sur les lésions qui déterminent cette forme de paraplégie ; qu'il me suffise de dire qu'il s'agit généralement, soit d'altérations scléreuses diffuses de la moelle, soit d'une compression spinale par une tumeur intra-rachidienne, ou par une pachyméningite ; en outre, dans les cas de ce genre, quand ils sont très caractérisés, la dégénération secondaire des faisceaux pyramidaux fait défaut ou bien est très légère ; c'est du moins ce qui semble ressortir des observations anatomo-cliniques recueillies jusqu'à ce jour.

"Je reviens à la clinique. La rigidité musculaire de cette forme de

paraplégie constitue bien une contracture ; elle est, en effet, pathologique, due à un mode de l'activité musculaire, et elle est stable, au moins à une période de son évolution. Mais, comme nous venons de le voir, cette stabilité est moindre que celle de la contracture de la paraplégie spastique d'Erb ; elle est entrecoupée en partie de contractions involontaires lentes constituant de véritables mouvements spasmodiques, et, à la phase de début, les troubles méritent moins d'être rangés dans la catégorie des contractures que dans celle des spasmes. Il en résulte que l'épithète de "spasmodique" conviendrait bien plus à cette variété de paraplégie qu'au syndrome dénommé "tabes dorsal spasmodique."

"La contracture dont nous nous occupons a pour substratum anatomique, comme nous venons de le voir, des lésions du système nerveux central ; ces lésions intéressent la voie pyramidale dont la perturbation se manifeste pendant la vie par le signe des orteils et par l'exagération des réflexes de défense.

"Me voici maintenant en mesure de répondre à la question que j'ai posée après avoir montré que la contracture vulgaire, liée à une altération de la voie pyramidale, a des relations étroites avec la surréflectivité tendineuse. Je peux affirmer qu'il existe aussi une contracture—différente, il est vrai, de la précédente par sa forme—déterminée par des lésions nerveuses centrales atteignant les faisceaux pyramidaux, et pourtant absolument indépendante de la surréflectivité tendineuse. En effet, chez les malades qui la présentent, les réflexes tendineux ne sont pas toujours exagérés, tant s'en faut ; ils sont souvent, soit normaux, soit affaiblis, soit même abolis. Les réflexes de défense, au contraire, sont non seulement toujours présents, mais ils atteignent une très grande intensité.

"Mes observations ont été confirmées sur tous les points par plusieurs neurologistes.

"Cette forme de contracture, surtout commune aux membres inférieurs, peut atteindre en même temps les membres supérieurs, où elle offre les mêmes caractères : rigidité avec mouvements spasmodiques, affaiblissement ou abolition possible des réflexes osso-tendineux, réflexes de défense très forts.

"Qu'on la considère aux membres inférieurs ou aux membres supérieurs, ce qui frappe surtout, ce sont ses liens intimes avec les réflexes cutanés de défense dont elle paraît dépendre, comme la forme habituelle de la contracture dépend de la surréflectivité tendineuse. Pour mettre ces traits en évidence et pour donner à chacune de ces formes de contracture—qui peuvent d'ailleurs s'associer—une dénomination qui la distingue, j'ai proposé d'appliquer à l'une le qualificatif de *tendino-réflexe* et celui de *cutanéo-réflexe* à l'autre."

A côté des formes types, il y a des formes qu'on pourrait appeler intermédiaires où l'on trouve les principaux caractères de la contracture cutanéo-réflexe (motricité volontaire très troublée, réflexes de défense très forts) bien que les membres inférieurs gardent d'habitude une attitude en extension. Précédemment, j'en ai montré un bel exemple en vous relatant l'Observation d'une paraplégie due à une compression par tumeur et guérie à la suite de l'intervention chirurgicale. Cette dernière forme comporte un pronostic moins sévère que la paraplégie spasmodique en flexion, laquelle correspond à un stade plus avancé de l'affection.

En France, ma manière de voir a été généralement acceptée et dans un article récent M. Foix [16] écrit ceci :

"*Contracture d'automatisme médullaire.*—C'est à mon maître Brissaud, dont la mort prématurée fut un deuil pour la neurologie française, que revient l'honneur d'avoir étudié en premier les contractures en flexion ; mais c'est M. Babinski qui le premier en a établi toute l'importance en montrant qu'elles avaient une séméiologie, une signification pathologique complètement différentes des contractures en extension.

" C'est en effet au sujet des paraplégies en flexion que M. Babinski a établi une distinction entre les contractures tendino et cutanéo-réflexes qui marque une date dans l'histoire des contractures.

" Nous ne chicanerons pas ici M. Babinski sur le mot plus ou moins heureusement choisi de cutanéo-réflexe. Il est évident que cette contracture n'a rien de cutané, puisque les réflexes qui la caractérisent peuvent être aussi bien provoqués par l'excitation de la sensibilité profonde que par celle de la sensibilité superficielle. Il n'en est pas moins vrai que la contracture en extension est avant tout caractérisée par l'exagération des réflexes tendineux et la faible intensité des réflexes d'automatisme appelés encore de défense.. Tandis que la contracture en flexion est caractérisée non seulement par l'exagération considérable des réflexes d'automatisme, mais encore par la diminution ou l'abolition des réflexes tendineux.

" A cette différence de séméiologie répondent des différences profondes d'étiologie, de pronostic, de signification physiologique.

"Voici une malade qui présente précisément cette contracture en flexion. Considérons-la un instant. Nous voyons d'abord quelle est son attitude. Ses jambes sont ramassées vers elle. Examinons-la de plus près. C'est une attitude de raccourcissement. Et ce raccourcissement comporte le triple retrait segmentaire que nous avons déjà deux fois rencontré : flexion du pied sur la jambe, de la jambe sur la cuisse, de la cuisse sur le bassin.

" Poursuivons plus loin notre étude. Les réflexes rotuliens sont faibles, il n'y a pas de clonus du pied. Par contre, ces réflexes d'automatisme sont très faciles à provoquer : voici le phénomène des raccourcisseurs, une ébauche de réflexe d'allongement, un réflexe partiel d'allongement croisé. C'est bien la dissociation décrite par M. Babinski.

" Comment peut-on interpréter cette séméiologie d'abord, cette attitude ensuite ?

" En ce qui concerne les réflexes d'automatisme, leur intensité implique une libération de la moelle inférieure. C'est là un fait qui n'est pas sans importance, car il indique en général des lésions plus profondes que celles qui s'accompagnent de contractures en extension. On voit assez souvent la contracture en flexion se substituer à la contracture en extension. Pendant quelque temps alors, il y a lutte entre les deux tendances et les deux réflectivités. Toujours la victoire de la flexion implique une aggravation de l'état du malade.

" Y a-t-il seulement *libération* de la moelle ? N'y a-t-il pas en outre irritation, *exaltation* de l'automatisme médullaire ? C'est une chose que, pour ma part, je crois, mais il est difficile d'en donner la preuve."

. . . . .

" Quant à la contracture en flexion elle-même, son aspect indique quelle en est la pathogénie. Elle n'est autre chose, en effet, qu'un phénomène des raccourcisseurs fixé."

Sauf sa remarque sur le terme cutanéo-réflexe, M. Foix est à peu près d'accord avec moi. Je ne trouve pas, soit dit en passant, que son objection soit juste : peu importe que les réactions motrices puissent être obtenues aussi par l'excitation des parties profondes ; il suffit que l'excitation de la peau seule puisse y donner naissance pour qu'on ait le droit de dire qu'elles sont cutanées. Mais c'est là un point tout à fait secondaire. Pour le fond de la question, M. Foix confirme mes observations.

Au contraire, les neurologistes anglais, en particulier MM. Walshe et Riddoch, expriment des critiques qui sont peut-être, au moins en partie, la conséquence de malentendus. Si je saisis bien ce qu'il y a de principal dans les idées de M. Walshe sur les réflexes d'extension et de flexion, voici en quoi elles consistent :

Les extenseurs et les fléchisseurs forment deux groupes soumis chacun à une forme spécifique d'activité réflexe ; elle est tonique dans l'un, clonique, phasique, dans l'autre. Le centre de cette activité a pour siège unique les noyaux spinaux, en ce qui concerne les fléchisseurs ; l'activité des extenseurs nécessite, pour se maintenir, la mise en jeu d'un autre appareil réflexe dont le centre occupe le mésocéphale, les noyaux

paracérébelleux probablement (centre des réflexes de posture).—Une lésion cantonnée dans le faisceau pyramidal exalte à la fois l'activité réflexe des extenseurs et celle des fléchisseurs et donne lieu à une paraplégie en extension. Une lésion siégeant au-dessus du mésocéphale ne produirait jamais une paraplégie en flexion.—Au contraire, une lésion de la voie pyramidale associée à une lésion occupant une des parties de l'arc réflexe, ayant pour centre les noyaux paracérébelleux, détermine une paraplégie spasmodique en flexion ; en effet, l'activité réflexe des fléchisseurs n'est pas affectée par l'interruption de cette voie puisque cette activité est d'origine uniquement spinale ; elle est même augmentée, n'étant plus freinée par une force antagoniste. De pareilles altérations donneraient lieu à une exagération des réflexes s'opérant toujours en flexion ; l'extension, quand elle s'observe, n'étant qu'un effet du relâchement des fléchisseurs, ou étant un allongement croisé, toujours secondaire, jamais primitive.—Les réflexes de défense sont d'autant plus forts (période de shock mise à part) que la séparation entre les centres spinaux et les centres mésocéphaliques est plus grande, que la libération de la moelle est plus complète.—Mais, pour qu'il se développe de la contracture, il faut que les muscles aient un certain degré de tonicité que n'atteignent pas, même après la période de shock, les muscles dans les cas de paraplégie consécutive à une section totale de la moelle ; la contracture implique la persistance de quelques connexions entre l'encéphale et la moelle.

A certains points de vue, cette conception pathogénique cadre avec la description clinique que j'ai faite antérieurement de la paraplégie en extension et de la paraplégie en flexion.

Mettons en regard les caractères symptomatiques tracés par moi de ces deux types de paraplégie et les données physio-pathologiques énoncées par les auteurs anglais.

PARAPLÉGIE SPASMODIQUE EN EXTENSION.	
(*a*) Stabilité de la contracture.	L'activité réflexe des extenseurs est à forme tonique.
(*b*) Réflexes de défense légèrement exagérés ou à peu près normaux.	L'activité réflexe des fléchisseurs a pour antagoniste celle des extenseurs.
PARAPLÉGIE EN FLEXION.	
(*a*) Instabilité relative de la contracture avec variations fréquentes liées à des mouvements alternatifs de flexion et d'extension et avec prédominance d'action des fléchisseurs.	L'activité réflexe des fléchisseurs est à forme clonique phasique.

(*b*) Exagération notable des réflexes de défense.

(*c*) Motricité volontaire profondément troublée.

(*d*) Les dégénérations secondaires peuvent être très faibles ou nulles.

L'activité réflexe des fléchisseurs n'est plus freinée par une force antagoniste.

Les réflexes de défense sont d'autant plus forts que la libération de la moelle est plus complète.

Pour que la paraplégie en flexion avec contracture se développe, les connexions entre la moelle et l'encéphale ne doivent pas être complètement rompues.

Mais il est certain qu'il y a aussi des divergences pouvant résulter de ce que le sens des termes employés n'a pas été suffisamment précisé. Il me semble que MM. Walshe et Riddoch, tout en reconnaissant l'intérêt qu'il y a à distinguer la paraplégie en extension de celle en flexion et en rappelant mes travaux sur cette dernière, n'ont pas bien saisi mes idées et qu'il y a là une confusion. Pour eux, la paraplégie spasmodique en flexion est réalisée quand à une paraplégie, serait-elle flasque, s'associent des réflexes de défense amenant la triple flexion, et c'est dans les cas de section complète de la moelle qu'on en observerait les exemples les plus typiques. Or, dans ma description de la paraplégie en flexion, j'ai fait intervenir l'élément *raideur* (contracture cutanéo-réflexe) ; cette rigidité, il est vrai, peut céder par moments au début ; mais plus tard elle devient relativement stable. C'est ce type que j'ai toujours eu en vue, celui d'ailleurs que d'autres neurologistes ont observé après moi et qu'on rencontre encore assez souvent dans la pratique habituelle, les cas de section totale étant tout à fait exceptionnels.

J'estime être en droit de maintenir mon opinion suivant laquelle ce type de paraplégie en flexion, avec contracture, réflexes de défense extrêmement exagérés, exagérés au maximum, est d'habitude liée à des compressions, des lésions scléreuses diffuses sans dégénération secondaire ou avec dégénérations secondaires minimes, ce qui ne veut pas dire que cet état soit incompatible avec des dégénérations secondaires marquées. A cet égard, les observations nouvelles, de guerre, si intéressantes qu'elles soient, n'infirment aucunement les observations anciennes.

Contre l'opinion de M. Walshe et de ceux suivant lesquels une lésion siégeant au-dessus du mésocéphale ne produirait jamais une paraplégie en flexion, on peut faire valoir l'Observation rapportée par MM. Pierre Marie et Foix [24] et intitulée : "Paraplégie en flexion d'origine cérébrale par nécrose sous-épidymaire progressive."

"Notre cas, disent les auteurs, est, croyons-nous, le premier cas anatomo-clinique de paraplégie en *flexion* d'origine cérébrale ; en tout cas, le premier dans lequel on ait observé la dissociation signalée dans certains cas par M. Babinski entre les réflexes d'automatisme dits de défense et les réflexes tendineux.

"Ceci est une notion importante au point de vue physiologique, car il n'existait pas chez notre malade de lésions mésocéphaliques, mais simplement une double lésion cérébrale. La suppression de l'influence des centres mésocéphaliques n'est donc pas indispensable pour que se produise l'automatisme médullaire et la paraplégie en flexion. Il n'est pas nécessaire non plus qu'il y ait lésion irritative comme dans le cas déjà signalé de M. Babinski (paraplégie en flexion par compression mésocéphalique) ; une simple lésion destructive suffit, en supprimant l'influence cérébrale."

A ce sujet, je rappellerai que dans mon travail de 1911 sur la Paraplégie spasmodique avec contracture en flexion, j'écrivais ceci, p. 135 : "Des lésions bilatérales de l'encéphale semblent pouvoir donner naissance à un syndrome analogue" [3].

Il faut s'attendre à la publication de nouvelles observations et à de nouvelles discussions. Le dernier mot sur cette question ne paraît pas avoir été dit.

* * * *

Dans une communication intitulée : "De la surréflectivité hyperalgésique" [8], nous avons relaté, Jarkowski et moi, trois Observations de Syndrome de Brown-Séquard, dans lesquelles nous avons été frappés par la présence d'un même phénomène dont voici les traits essentiels : une excitation telle que le pincement de la peau du côté de la lésion, où il y a de l'hyperalgésie, sans être suivie d'aucune manifestation de ce côté, donne lieu du côté opposé à une réaction motrice brusque, en même temps qu'elle détermine des grimaces et une inspiration bruyante (phénomènes analogues aux "pseudaffective reflexes" observés par Sherrington chez les animaux décérébrés).

Dans un travail ultérieur, "Automatisme et hyperalgésie dans l'hémiplégie cérebrale" [9], nous avons relaté les faits suivants : chez certains hémiplégiques présentant de l'hyperalgésie, l'excitation des téguments du membre inférieur est suivie d'une réaction motrice du membre supérieur du côté sain, différente suivant qu'on excite le côté sain ou le côté malade. Dans le premier cas, la main se porte sur le point excité comme pour le protéger. Dans le deuxième, le membre supérieur se soulève, la main se porte sur la tête et vient s'appliquer soit à sa partie antérieure, soit à sa partie postérieure. Dans certains cas, nous avons

été frappés par la constance avec laquelle ces réactions se produisaient. On pouvait à volonté, en pinçant alternativement les deux côtés, faire exécuter à la main saine des mouvements en sens inverse : la main était-elle appliquée sur la tête à la suite du pincement du côté malade, on obtenait son déplacement vers le membre inférieur du côté sain en pinçant la jambe saine ; et si alors on pinçait la jambe du côté malade, le bras s'élevait de nouveau et la main se portait sur la tête.

Ces réactions motrices diffèrent cliniquement de celles que nous avons étudiée dans notre Conférence. Nous les rapprochons des réflexes de défense, mais nous les en distinguons. Les unes et les autres peuvent d'ailleurs être associées.

Nous pensons que les réactions observées chez les malades qui font l'objet de notre travail sur la réflectivité hyperalgésique sont des réflexes ayant leur centre dans l'encéphale.

Quant aux mouvements de la main vers la tête constatés chez les hémiplégiques dans notre Note sur l'automatisme et l'hyperalgésie, nous sommes portés à croire qu'il s'agit là d'un acte automatique déclenché par la sensation spéciale qui résulte de l'hyperalgésie, sensation nouvelle, non encore éprouvée, insolite et occasionnant ainsi une surprise, un état d'anxiété que traduit la physionomie du malade, bien que sa conscience puisse être considérablement amoindrie.

Nous avons cru devoir signaler ces phénomènes dont on trouvera la description détaillée dans nos publications. Mais nous n'y insisterons pas davantage, faute de temps et parceque, en le faisant, nous sortirions des limites de notre programme.

* * * *

Je me suis proposé de traiter dans cette Conférence la question des réflexes de défense surtout en clinicien, en neurologiste. Je ne crois pas cependant pouvoir la terminer sans vous dire quelques mots du mécanisme de ces réflexes, dont il a été déjà question, du reste.

Vous avez vu que MM. Marie et Foix ont insisté sur la présence des réflexes d'extension croisée observés par eux chez certains sujets atteints de lésions de la voie pyramidale. Les rapprochant du " crossed extension reflex " de Philipson, ils arrivent à cette conclusion que les mouvements réflexes dits de défense sont des mouvements du même ordre que les mouvements du stepping reflex et constituent des manifestations de l'automatisme spinal de la marche. Les neurologistes anglais contestent l'exactitude de cette conception ; ils soutiennent que chez l'homme, dans les sections totales de la moelle, les excitations nociceptives d'un côté, quand elles provoquent l'activité des extenseurs du côté opposé, ne

donnent lieu qu'à des contractions légères sans déplacement des divers segments du membre, et que les mouvements alternatifs rythmés qu'on observe chez le chien spinal font ici défaut.

M. Foix, dans une publication récente à laquelle j'ai déjà fait des emprunts, semble faire quelques concessions tout en maintenant en grande partie son opinion première. "Il est possible, dit-il, que l'automatisme de défense entre pour une part dans la pathogénie de ces réflexes, mais, pour la majeure part, ils se rattachent à l'une des fonctions essentielles de la moelle, c'est à dire à l'automatisme de la marche."

J'ai cherché précédemment à faire ressortir la distinction capitale qu'établissent les auteurs anglais entre le groupe des fléchisseurs et celui des extenseurs soumis chacun à une forme spécifique d'activité réflexe : les réflexes d'extension seraient des réflexes de posture ; les réflexes de flexion seraient des reflexes cloniques, phasiques. C'est dans le groupe de ces derniers réflexes que rentrent pour la plus grande part ce qu'on appelle les réflexes de défense.

La conception fondamentale des neurologistes anglais, issue des idées de Jackson, de Sherrington, est que ces réflexes de flexion tels qu'on les observe à l'état pathologique traduisent la libération de la moelle par rapport aux centres supérieurs.

Les faits observés cadrent fort bien pour la plupart avec cette conception. Toutefois, sans en contester la justesse, on peut se demander si, dans la genèse des phénomènes en question, l'élément "irritation" ne peut pas jouer aussi un certain rôle.

C'est une idée que M. Foix tend à admettre, comme on l'a vu précédemment.

Ce fait que les réflexes de défense m'avaient paru dès mes premières observations particulièrement intenses dans les cas de compression de la moelle et de sclérose spinale sans dégénération secondaire m'avait déjà conduit autrefois à cette même idée.

A l'appui de cette manière de voir on peut invoquer encore d'autres faits sur lesquels nous avons déjà insisté. On peut observer parfois—nous le rappelons—des sujets atteints de lésions spinales qui, après avoir présenté une paraplégie plus ou moins marquée, paraissent complètement rétablis : la motricité est redevenue normale, la sensibilité est intacte, il n'y a pas de perturbation des sphincters, et cependant il y a persistance très nette du signe des orteils et de la flexion réflexe du pied. Sauf ces derniers phénomènes, le fonctionnement du système nerveux semble absolument normal. Est-il permis de soutenir en pareil cas qu'il y a libération de la moelle ? Ce ne serait alors qu'une libération relative aux reflexes de défense. L'état pathologique de ces réflexes ne se

comprendrait-il pas mieux dans des cas de ce genre si l'on admettait qu'il est sous la dépendance de l'irritation des centres nerveux produite par le reliquat de la lésion ?

Considérant maintenant la question d'un autre point de vue, je soumettrai quelques idées à vos réflexions.

Au début de cette Conférence, j'ai tracé un parallèle entre les réactions motrices consécutives aux excitations périphériques suivant qu'elles sont pathologiques ou physiologiques. Il résulte de ce que j'ai dit que les premières peuvent être considérées comme l'exagération des secondes, ou plutôt les secondes comme la réduction des premières : de part et d'autre, en effet, on observe le phénomène de la triple flexion avec contraction du tenseur du fascia lata ; mais ce qu'il y a de spécial aux réactions physiologiques c'est qu'on ne les obtient que par l'excitation de la zone plantaire et que les mouvements sont plus rapides et moins amples. A l'état pathologique, la triple flexion (seul mode de réaction que j'envisage ici) semble bien pouvoir être interprétée comme un retour à un état ancestral : la partie excitée fuit l'objet vulnérant (retrait du membre, raccourcissement) et une excitation peut déterminer, loin du point où elle a eu lieu, un mouvement de fuite ; c'est ainsi que la triple flexion peut être provoquée par excitation de l'abdomen ou du thorax. A l'état physiologique, ces réactions ancestrales se sont maintenues, mais ont subi des modifications importantes. Comment le comprendre? On pourrait dire que lorsque les centres supérieurs ont asservi les centres inférieurs, ceux qui correspondaient aux centres spinaux, ils ont inhibé les réactions susceptibles d'être nuisibles à l'individu et ont laissé subsister, en les adaptant à ses besoins, celles qui sont capables de lui servir. Or, il est évident que la triple flexion consécutive à une excitation de la jambe, de la cuisse ou de l'abdomen ne pourrait avoir que des inconvénients ; cette réaction a donc été supprimée. Que sous l'influence d'une irritation nocive de la plante du pied continuellement en contact avec le sol, la triple flexion s'opère, même indépendamment de la volonté, cela ne peut être qu'utile ; cette réaction a donc été conservée. Mais il y a intérêt aussi, au point de vue de la marche, à ce que la réaction ne soit pas de longue durée ; aussi la décontraction est-elle rapide au lieu d'être lente. On saisit ainsi les raisons pour lesquelles, à l'état physiologique, les réactions motrices qui me paraissent ressortir aux réflexes de défense, s'effectuent avec rapidité et ne se produisent que lorsque les excitations portent sur la région plantaire.

Il me semble intéressant de rappeler à ce propos que dans les sections totales de la moelle, après la période de shock, lorsque les réflexes

cutanés reparaissent, la région plantaire est seule réflexogène pendant un certain temps.

Comparons maintenant le réflexe des orteils aux réflexes précédents. Si à l'état pathologique la réaction habituelle des orteils, l'extension, peut être rapprochée, en ce qui concerne son mécanisme, de la triple flexion, à l'état physiologique le mouvement des orteils, la flexion, semble avoir une autre signification que la triple flexion du pied, de la jambe et de la cuisse. M. Riddoch fait observer que la flexion réflexe des orteils fait partie du stepping-reflex, et qu'elle accompagne l'extension de la cuisse, de la jambe et du pied. Mais il est à remarquer qu'à l'état physiologique chez l'homme, l'excitation de la plante du pied, qui provoque la flexion des orteils, détermine du même côté la triple flexion du membre inférieur et il en résulte une quadruple flexion. Cette flexion des orteils ne serait-elle pas aussi le témoin d'une réaction ancestrale, ayant apparu toutefois à une période du développement plus avancée que les réflexes de défense dont il a été précédemment question, période où les orteils servaient de griffe? Cette réaction avait aussi en partie la protection pour but, mais c'était un mode de protection différent de celui qui est réalisé par les réflexes de défense primitifs ; il ne s'agit plus d'une fuite localisée, d'une retraite en face d'une offensive ; ce mouvement de griffe vis à vis d'une aggression constitue une contre-offensive, mode de protection d'un ordre plus élevé ; on conçoit du reste fort bien qu'un animal cherchant à se défendre combine l'attaque avec la fuite. On saisirait ainsi la quadruple flexion à l'état physiologique : la flexion de la cuisse, de la jambe et du pied ressortissant aux réflexes de défense primitifs, la flexion des orteils étant l'expression atavique d'un réflexe de préhension.

Cette conception permettrait de comprendre pourquoi l'extension des orteils n'est pas toujours associée à la triple flexion ; suivant que dans le domaine des orteils, le réflexe de fuite l'emportera, ce qui est la règle à l'état pathologique, sur ce que nous appelons le réflexe de préhension, ou bien sera dominé par lui, on obtiendra l'extension ou la flexion des orteils.

Je rappellerai à ce propos que M. van Woerkom, dans le travail cité plus haut, fait ressortir que " le gros orteil est construit dans certains stades de la vie intra-utérine pour remplir une fonction de préhension." Cet état qui chez les autres primates est perpétuel, est passager chez l'homme.

Est-il nécessaire d'ajouter qu'il s'agit là pour une grande part d'hypothèses!

* * * *

Dès le début de mes recherches sur le phénomène des orteils, j'avais eu l'occasion de le constater chez des nourrissons, et il m'avait semblé

qu'il persistait approximativement jusqu'à la période où l'enfant commence à marcher, ce qui s'explique quand on se rappelle quel est l'état du système pyramidal à cette époque de la vie : on peut dire que l'enfant est atteint d'une paraplégie—curable—comme on peut dire aussi que chez lui la moelle n'est pas encore sous la domination de l'encéphale.

D'après Léri [20], à la naissance l'extension des orteils est la règle ; la flexion l'exception. L'extension disparaît en général, chez l'enfant normal, vers 5 ou 6 mois, mais il y a des variétés individuelles ; il peut y avoir une période de transition assez prolongée, marquée par des alternatives de flexion et d'extension et souvent par l'extension unilatérale.

Des recherches nouvelles de Bersot [12], de Lantuejoul (communication orale) ont montré qu'il y avait lieu de rectifier un peu les données précédentes : à la naissance, puis pendant un laps de temps d'une durée assez courte, les orteils réagissent en flexion et ce n'est qu'ultérieurement que l'extension apparaît. Cela surprend d'abord, mais n'est pas contradictoire si l'on admet que la flexion des orteils, réaction physiologique il est vrai, est le reliquat d'une réaction ancestrale et si l'on se rappelle que chez l'adulte on peut observer un réflexe en flexion chez des sujets atteints de lésions avérées de la voie pyramidale.

En ce qui concerne la flexion réflexe du pied, on la constate aussi chez l'enfant, ainsi que l'a établi une de mes élèves, Mlle Rosenblum, qui a fait de cette question l'objet de sa Thèse inaugurale ; mais l'extension du gros orteil subsiste d'habitude plus longtemps que la triple flexion.

Je vous signale avant de terminer un travail de M. Minkowski ayant pour titre : " Sur les mouvements, les réflexes et les réactions musculaires du fœtus humain de 2 à 5 mois, et leurs relations avec le système nerveux fœtal " [25].

J'extrais de cet article (p. 1113) le passage suivant : " On peut dire en général que chaque partie des téguments peut servir de zone réflexogène à des réactions motrices très variables, proches et lointaines, ayant la tendance à se généraliser plus ou moins à tout l'organisme fœtal."

Cette donnée est à rapprocher de ce que nous avons dit précédemment sur la possibilité de provoquer parfois, à l'état pathologique, des réflexes des orteils et du pied en excitant les téguments de l'abdomen et du thorax.

Messieurs, comme vous venez de le voir, l'étude des réflexes de défense soulève des problèmes de phylogénie et d'ontogénie, et à cet égard elle est déjà fort intéressante ; mais elle l'est surtout pour le neurologiste. Ces réflexes constituent un chapitre important de la pathologie du système nerveux.

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A STUDY OF THE SHERRINGTON DECEREBRATE ANIMAL IN THE CHRONIC AS WELL AS THE ACUTE CONDITION.

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[1] In general the experimental work was done by H. C. B., and Chapters II, III and VI (*b*) were written by him. The semi-decerebrations and all the anatomical examinations were made by W. G. P., and Chapters IV, V and VI (*a*) were written by him.

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INTRODUCTION.

THE researches on which this paper is based were commenced originally in a search for a preparation which would allow experiments on the origin of surgical shock, and also on the effect of temperature on the resistance to infection in animals not under an anæsthetic and yet without there being any possibility of pain. The Sherrington preparation seemed ideal for this purpose, since the question of any conscious sensation could be completely excluded, and in addition the preparation would remain quiet during experimentation. The main object has, therefore, been to develop a technique which would allow the preservation of the decerebrate animal for many days, in spite of the removal not only of the cerebrum, but also of the basal ganglia and most of the mid-brain. This has necessitated the use of 124 animals, and in the course of the work some points of interest have arisen in connection with the reflexes and the histological anatomy. In many experiments our data are not as complete as we would have wished, but it was found that the process of examining the animals diminished their chance of survival and consequently the observations had to be curtailed, if the main object of the research was to be attained.

In spite of these difficulties a certain number of important facts were demonstrated. One of the most noticeable was the very remarkable similarity between the decerebrate preparations which had been kept "alive" for two or three weeks, and the acute preparations described by Sherrington on examination an hour or so after the operation. The decerebrate rigidity often continues (with only brief intermissions) for weeks, so that there can be no possibility of the condition being due to stimulation of the cut nerve fibres at the site of operation, and since in this time the damaged nerves are undergoing degeneration it is possible to exclude definitely some structures from any participation in this reflex. On the other hand, the chronic preparations do show certain

definite differences from the acute; for instance, after the first two or three days a small percentage of the animals will occasionally make definite sounds, and these sounds appear to be reflex since they occur usually as the result of some definite stimulus. The most common of these sounds was purring occurring immediately after the stomach had been filled with milk by a stomach tube, while mewing has only been observed in two animals, and in these it occurred only once or twice and could not be made to recur by applying stimuli which would be painful to a conscious animal.

Extensive histological studies have only been possible on a few of the preparations, but in these the results are of interest since we believe that never before have preparations been maintained in a sort of life so as to allow degeneration to occur after such complete removal of all the higher nervous centres. In many other cases the nervous tissue was useless for detailed examination as the result of incubation for some hours after death and consequent rapid post-mortem changes.

Chapter I.—Historical Note on Decerebration.

The method of removing parts of the brain in order to study function in the central nervous system has been employed since Rolando's experiments on birds in 1809. Flourens, indeed, succeeded in keeping pigeons alive for months after the removal of the fore-brain. But Longet [32], in 1842, first discriminated carefully as to what brain structures he actually removed. He noticed that many "reactions" remained if he removed all of the brain down to and including the colliculi—"chose remarquable!"; but that after removal of the pons all reactions disappeared, excepting only respiration and circulation.

Goltz kept three decerebrate dogs alive for months. The brain-stem of one animal most carefully studied was examined by Gordon Holmes [21], who found that a considerable amount of thalamus and all the cranial nerves were intact, although there seemed to be some softening of the corpora quadrigemina. There was no loss of temperature control and the animal shivered in a cold room. It could walk and would eat when brought close to food. Rothmann [51] [52] likewise produced a chronic preparation, a dog from whom all or most of the brain above the optic thalamus was removed. This animal ate and drank normally, walked and ran and showed a limited ability to learn. He likewise had normal temperature control and apparently normal muscle tone. Karplus and Kreidl [25] extirpated the hemispheres of monkeys and

kept one alive as long as twenty-six days. More recently, Dusser de Barenne [2] has kept one cat alive six months, and another animal eleven months, after removing the fore-brain. A careful examination by Brouwer [7] of the post-mortem material showed the thalamus, mid-brain, and rhinencephalon to be intact in one, and most of the thalamus and mid-brain in the other. These preparations did not show decerebrate rigidity and were able to maintain a normal temperature. Only the animal with a portion of the fore-brain intact would eat spontaneously.

As indicated briefly above, in all previous *chronic* decerebrate preparations much of the thalamus was intact as well as the mid-brain. The animals possessed normal temperature control and have been able to execute complicated co-ordinated movements.

Decerebration at the level of the mid-brain was shown by Sherrington in 1896 to produce "decerebrate rigidity." This condition in *acute* preparations has been the subject of much study since that time by Horsley, Thiele, Weed, Magnus, Cobb, *et al.* Their conclusions will be discussed in another part of this communication. Recently, signs and symptoms in a group of patients considered to be analogous to decerebrate animals have been described by Wilson [63]. Riddoch and Buzzard [49] have also described such symptoms in man.

Boyce [6], in 1895, removed the brain on one side down to the middle of the mesencephalon and kept the animals (cats) alive as chronic preparations. His principal interest was in the descending degenerations thus produced. Probst [46], in 1904, made sections through one lateral half of the mid-brain without removing any tissue and studied the general behaviour of the animals as chronic preparations.

This brief sketch makes no pretence to enumeration of all of the valuable contributions to neurology made by this experimental method. In general, preparations produced by decerebration at higher levels and extending down as far as the medulla oblongata have been studied as *acute* experiments. In the case of all previous *chronic* experiments, the level of removal has been at least well above the mid-brain and most of the thalamus.

Chapter II.—Technique.

The animals used have been cats in all cases. The general procedure has been to decerebrate the animals aseptically under an anæsthetic and then to keep them under conditions which will maintain by artificial means their temperature constant. In the main

the technique has followed the lines described by one of us (H. C. B.) [4] in a preliminary communication,[1] but as it has been modified in details it will be advisable to give here a full description. The whole process is founded on Sherrington's original (and older) method developed in 1896 [53] [54].

(a) Operative.

Pure chloroform has been used as the anæsthetic since we have had no success with ether. The preparations have considerable difficulty in getting rid of mucus and this probably accounts for the difficulties we have had. Subcutaneous injection of 0·5 mgm. of atropine has been given immediately after induction of anæsthesia in some animals, perhaps with beneficial effect. During the actual decerebration a total cessation of respiratory movements for a short while is not uncommon, and causes the loss of some animals. To overcome this intratracheal insufflation has been tried both with chloroform and ether. With chloroform insufflation we have had some success, but the greater irritation to the trachea and the consequent risk of infection seem to more than counterbalance the diminished risk of the actual operation. Cessation of respiration is less liable to occur if the animal is deeply anæsthetized at the time the section is made, so that with a good anæsthetist trouble of this kind is rare, even with an ordinary inhalation method, and it is this that we have mostly used.

The skin on the back of the head is shaved, cleaned and painted with an alcoholic solution of iodine, and in the later technique the animal is then turned over and the front of its neck is also shaved. A small incision is made (1 to 2 cm. in length) in the mid-line at the level of the thyroid cartilage, and from this both carotid arteries can be reached; a thick ligature is passed around each of them, and is then tied to form a loop so that traction can be made on the vessels to obstruct the blood-flow as desired. These two loops are brought out through the middle line and then the wound is closed with two or three waxed silk sutures. Hæmostat forceps hanging on these loops during the actual process of decerebration will prevent most of the bleeding and allow much more accurate work. It does not seem necessary to take any aseptic precautions after this neck wound has once been stitched up, and we have had no serious infection of these wounds.

The animal is then again turned over and an incision made on the

[1] In the protocols "earlier method" indicates that the operation was performed as described in this communication.

back of the head. A skin flap is turned back on one side, the temporal muscle is separated from the bone, the skull is trephined and the hole enlarged to a good size. While the actual decerebration is performed the weights on the carotid are allowed to hang free and constrict the vessels and the anæsthetist compresses the vertebral arteries just below the transverse processes of the atlas. The dura is opened and with a blunt spatula the occipital lobe on the near side is removed so as to bring into view the corpora quadrigemina. The division across the brain-stem can then be made at any desired level; this is done with the same blunt spatula, carrying the cut right through the brain to the base of the skull. It has proved much more satisfactory to make absolutely certain of preserving the pituitary gland intact, as will be explained later, and this has been attained most easily by the careful choice of the plane of the section and by carrying a horizontal cut forwards with a specially bent and rather blunt scalpel, starting from the transverse incision and passing forwards through the base of the brain a millimetre or two above the level of the pituitary. The whole of the brain matter above these two cuts is then scooped out and the cavity is lightly plugged with cotton wool. After this the vertebral arteries may be released and a little later the carotid blood-flow may be allowed to return. The whole procedure of removing the brain should only take about a minute or two.

The packing in the cavity is left for five or ten minutes and is then carefully removed. If there is any bleeding a small pad of muscle is put over it and packing is repeated and maintained for another five minutes. When the cavity is quite dry the closing of the wound is commenced. It is important to obliterate the large dead space of the cranial cavity in order to minimize the chance of infection. This has been done usually by filling it with a mixture of equal parts of vaseline and paraffin wax (melting 55° C.), the mixture setting at about 45° C. It is sterilized by heating to 140° C. for three-quarters of an hour on three successive days. If the hæmorrhage has been difficult to stop it is usually safer first to spread over the base of the skull a thin layer of gauze soaked in saline, the end of the gauze protruding through the wound, the temporal muscle being split vertically so as to make this easier, and then pour in the wax at a temperature of about 47° C., allowing it to set in the cranium. The wax does not stick to the wet gauze, so that when the wax is set the gauze may be gently withdrawn, or if hæmorrhage is feared it may be left in place until the following day. In the latter case a corner of the gauze may either be allowed to

protrude through a counter-incision in the skin, or it may lie just beneath the skin which has been closed by a suture above it, so that on the next day the stitch may be removed and the gauze withdrawn without any trouble. It is probable that it is best to leave always a little gauze in place while the wax is setting, since on removal it leaves a small cavity and so allows room for some swelling of the remaining parts. In the earlier experiments where the whole brain matter to the level of the tentorium was scraped away trouble from this factor was not conspicuous, but with the modification of the operation as here described a post-operative rise in intracranial pressure may play a more important rôle.

In the few animals in which only one hemisphere has been removed the use of wax has proved unsatisfactory, probably owing to the much greater chance of swelling of the remaining parts in these animals. In the unilateral decerebrations in consequence the cavity has been merely filled with saline and it is conceivable that this might also be satisfactory even in the complete decerebrations. The other variations in the technique in the unilateral operation are described later (Chapter IV), since all these animals have been operated on by W. G. P. An attempt has also been made to get rid of the dead space in the animals by removing the whole cranial vault and drawing together the two temporal muscles over the base of the skull. Unfortunately it is not possible to make these muscles cover the space completely, nor is it possible to leave a smooth surface at the base of the skull without opening the nasal sinuses, and in our experience this had led to an infection of the wound with a regularity not seen in the paraffin method. For experiments lasting only three or four days, however, it is satisfactory.

The main difference between the later technique and the earlier one previously described is the horizontal section just above the level of the pituitary gland, allowing the blood-supply of this gland to remain intact. The contrast between the two methods may be seen by reference to figs. 9 and 10, which show photographs of a brain-stem operated on by the later method and comparing with them fig. 22, which illustrates the brain-stem left by the older technique. As in the earlier experiments the stalk of the gland was cut across, the blood-vessels supplying the anterior lobe must have been divided, and the gland itself may easily have been damaged and perhaps subjected to some pressure. In spite of this several animals survived for periods of two or three weeks, but as a rule they would not live more than three or four days. In these death was preceded usually by convulsive movements without signs of

infection, or else was due to broncho-pneumonia. The convulsions occurring within three or four days were apparently similar to those described by Cushing [12] [13] as the result of removal of the pituitary, and consequently the modified operative technique was developed. This necessitates a more ragged incision with greater hæmorrhage, so that temporary control of the carotid arteries had to be also adopted. Following this change in the technique death on the third or fourth day preceded by convulsions has no longer been seen, and the animal's resistance to broncho-pneumonia has also seemed greater, but on the other hand, many more animals have been lost during the first day from reactionary hæmorrhage, and infection of the wound itself has also been more common.

The later technique has also given rise to some trouble, since the changed slope of the section has often been overdone, resulting in damage to the fifth nerve. Such damage must be avoided since it leads to the development of ophthalmia and pressure sores around the mouth, complicating the nursing and greatly increasing the risk of broncho-pneumonia.

(*b*) *Post-operative.*

The wound requires no covering, especially if it be stitched with waxed silk to prevent infection tracking inwards along the sutures, which may otherwise occur if the animal be kept in a bath. The wound may be left dry or covered with mercury ointment.

The main difficulty to be overcome is the maintenance of a constant temperature. For the most part the animals have been kept in a water bath, through which water was kept circulating and in which they were supported on a sling three-quarters immersed in the water. Stirrers maintained a constant mixing of the water, and a toluol regulator maintained the bath with a variation of only 0·2 to 0·4 C. in twenty-four hours at its best. Unfortunately, it often fell below this standard, as owing to post-war conditions the gas pressure sometimes fell so low as to be incapable of heating the large volume of water circulating through the bath.

In a bath the preparation readily gains heat from or loses heat to the circulating water, so that its rectal temperature rarely differs from that of the bath by more than 1° C. and practically never by more than 1·5° C. The bath has been usually kept at a temperature between 38° and 39·5° C. This method is possibly the simplest that will allow the maintenance of a constant body temperature in a preparation where

the metabolism shows rapid variations, as it must in any which happen to show strong running reflexes. No ill effects from the prolonged immersion in water have been seen, even after two or three weeks, except a gradual shedding of the hair.

The disadvantages of the bath method are obvious, and it is this method that is mainly responsible for the paucity of our observations on the reflexes. Rough examination of the animal is possible as it is turned each day in the bath to avoid pressure sores, but in order to make any careful examination, it has to be taken out, washed in hot water, washed again with alcohol, roughly dried with a towel and finally dried in a hot incubator. Even with this technique, which requires four or five hours, the body temperature is apt to drop to 35° C. or lower, and though no ill results are noticed at the time, pneumonia often supervenes. Consequently any such examination will greatly decrease the preparation's chance of survival.

Owing to this many attempts have been made to keep them in an incubator. An ordinary incubator is useless, since the heat loss varies with the moisture in the air. Haldane [18] has shown the importance of the wet bulb temperature, but even an incubator controlled on a wet bulb basis is insufficient. The reason for this is that a very exact balance between heat loss and heat production has to be attained in these animals, and once this balance is upset the discrepancy tends to grow, since it is probable that in these preparations the metabolism falls with fall of body temperature instead of showing a compensatory increase. An incubator method has, however, proved possible by using an incubator heated by live steam escaping within it, so that heating occurs through condensation on its walls. In this way the wet and dry bulb temperatures are identical, the air being completely saturated with moisture. Even in such an incubator the control has to be altered during the first few days to match the gradual loss of the insulating action of the fur as it becomes penetrated with moisture, or this variation must be overcome by destroying these heat insulating properties of the fur by soaking the animal immediately after operation in petroleum oil. Under these conditions the animal loses heat mainly by radiation and conduction and usually keeps a rectal temperature about 4° C. above that of the incubator, so that this should be kept at about 34° or 35° C. The proper mixing of the air is ensured by an electrically driven fan. Further details of incubator experiments are given in Chapter III.

Food is given twice a day by stomach tube, a full-size cat requiring

about 100 c.c. of milk at each feed. Great care must be taken to keep the mouth, eyes and nose clean, and the animal must be placed in a position which would be comfortable if it were conscious.

The chief causes of failure are infection, usually respiratory, less commonly infection of the wound, post-operative hæmorrhage, and in the earlier technique probably also pituitary insufficiency. No testicular atrophy nor adiposity has, however, been observed. One animal (previously reported) lost 10 per cent. of its weight in a week, but another (cat II) after twelve days "life" showed no change whatever in its body weight. Further experiments on the functioning of the pituitary in these animals are planned.

The prevalence of pneumonia in these preparations is of some interest in that it was commoner if the animals had been previously exposed to conditions giving them a low body temperature, even if this occurred a considerable time after their anæsthetization. An instance of this is seen in the case of cat II, which is described later.

Chapter III.—Chronic Decerebrate Preparations.

(*a*) *Details of Two Preparations.*

The characters shown by these animals can be best illustrated by recording a few examples in more or less detail and then giving a more general description. The question of the individual peculiarities in relation to the exact site of the section is a difficult one and will be considered later.

Animal I.—Young castrated male. Post-mortem examination, p. 239. 0·5 mgm. atropine subcutaneously after anæsthesia induced. Right carotid tied, left occluded temporarily. Trouble from hæmorrhage which was eventually stopped after using a cautery and leaving in muscle and cotton-wool plugs. Some cotton left in under wax. Section by the later technique with preservation of the vascular supply to the pituitary. Kept on a warm table for three hours it developed a hæmatoma from reactionary hæmorrhage during this time. Five hours after operation when in bath had moderate rigidity[1] and moderately brisk pinna reflexes. Bath temperature 39·4° C. Rectal temperature 39·8° C.

Second day. Conditions much the same. Good corneal reflex on left side but none on right.

Third day. Condition much the same. Respiration rate only 17.

Fourth day. All reflexes more sluggish. Rigidity still fair.

Fifth day. Reflexes as before. Rigidity stronger and fore paws kept

[1] Rigidity refers to the extensor rigidity of the limbs described in decerebrate preparations by Sherrington unless otherwise stated.

extended and held rather backwards towards the tail. When turned on mattress slight kicking and extrusion of claws. Bath temperature 39·2° C. Rectal temperature 37·8° C.

Seventh day. All reflexes more brisk. Rigidity fairly good. Respiration rate 19. Sores developing in mouth.

Ninth day. Pinna reflexes more brisk. Vigorous shaking of the head now present on blowing in the ear. Licking of lips and nose now present after feeding. Rigidity very variable, being either very good or else animal in flexed and fairly flaccid condition.

Eleventh day. Reflexes still improving. Rigidity almost absent in the morning but on turning the animal it became extremely marked. The limbs are moved somewhat if the pinna is twisted. If traction is exerted on the front paws there is a movement of retraction and flexion of the limb with extrusion of the claws.

Thirteenth day. Ophthalmia of the right eye now well advanced. Rupture of cornea. Condition as before, but when lying on left side has a position in which the fore limbs are rigid and extended (left more than right) and in which the left hind limb was also rigid and extended, but the right hind limb was rigid in a flexed position. Hind limbs now show retraction when pulled upon as well as the fore limbs, but there is no extrusion of claws in the hind limbs. If animal is stimulated by twisting the ear the head is raised, being bent either to the left or right according to which side it is lying on. No acoustic reflex present now or at any other time.

On fourteenth day as before. Crossed reflexes easily obtained in hind limbs. If right limb is forcibly flexed it stays flexed and then on pinching left limb the left is flexed and right extended and vice versa. On cleaning the left eye the animal moves its head, extending it dorsally as though objecting. General appearance of movement is that of a pseudaffective reflex.

Fifteenth day. Respiration rate 12 only.

Seventeenth day. Respiration rate 16. Reflexes much as before but very variable.

Eighteenth day. Found dead.

Animal II.—Female. Post-mortem examination, p. 247. Weight, 2·45 kilos. Old method used and the cranial cavity scraped clean to the tentorium. Kept in incubator for one hour and then put into bath. Eight hours later fed, 100 c.c. of milk. Rigidity then good and pinna reflexes and corneal reflexes brisk. On following day these reflexes still brisk, respiration rate 20, bath temperature 39·2° C., rectal temperature 38·1° C.

After two days reflexes more brisk. Acoustic reflex now present; animal shakes its head slightly in response to loud noises.

Fourth day. Reflexes not quite so brisk; rigidity still good.

Fifth day. Vomited after the morning feed.

Sixth day. Reflexes much more brisk and rigidity very good. When lying on right side moves head slightly when hands are clapped; with high note of

a whistle lifts head up from the rest, bending it to the left. When lying on left side acoustic reflex scarcely noticeable, since the head is pressed downwards to the left.

Seventh day. Reflexes much more brisk, especially acoustic. If lying on right side now lifts head well up when anyone walks into the room, unless on tiptoe. Very brisk response to slight scratching noises. Pushes head downwards as before in response to sounds if lying on the other side.

Eighth day. Bath outlet choked. Animal taken out and dried during cleaning of the bath. During the drying, temperature fell to about 34° C. and remained subnormal about two hours. Weight when dry 2·4 kilos. Rigidity fairly good but not so strong as previously, and animal does not remain well in a sitting position as do most preparations. Acoustic reflex confined to head and neck movements. On touching the animal running movements are developed with strong movements of the front limbs and only slight in the hind limbs. Returned to the bath after eight hours.

Ninth day. Keeps eyes open, though previously they have been kept shut. On whichever side it is lying the upper fore limb is held passing forwards and downwards across the other, the lower fore limb passing somewhat backwards and upwards. This position is a very characteristic one and is seen in a large percentage of the preparations.

Eleventh day. When lying on left side responded to stimulations such as twisting of the ear, by kicking and some slight movement of the head. Rigidity intermittent and less marked than before.

Twelfth day. When being turned on the mattress kicks vigorously. Taken out of the bath in the evening and dried preparatory to Physiological Society meeting at Oxford. During drying temperature fell to 36° C. and remained subnormal for several hours.

Thirteenth day. Weight when dry 2·45 kilos. Respiration rate 24. Reflexes very brisk as before and kicking movements when the animal is stimulated. During most of the time the animal did not have a typical extensor position but remained moderately rigid in a semi-flexed posture and with a rigid flexion of the ankle-joints of the fore limbs. Temperature fell again to 36° C. during the afternoon when exhibited at the Physiological Society. Replaced in bath in the evening. Animal had sores from friction under armpits and during replacing in the bath made inco-ordinated attempts to reach the sores with its head and hind limbs.

Fourteenth day. Respiration faster. Animal kicking a lot when touched.

Fifteenth day. Respiration 66. Reflexes very poor.

Sixteenth day. Respiration 44. Reflexes slightly better.

Seventeenth day. Respiration 32. Reflexes good, except for acoustic, which has been absent since the fourteenth day.

Twentieth day. Respiration 24. Acoustic reflex present again for the first time since pneumonia began. Fore limbs rigid, extended and without movements. Hind limbs have a curious slight walking movement even when animal is not touched.

Twenty-first day. Kicking movements when stimulated. Made occasionally a curious sound like an inco-ordinated mew.

Twenty-second day. Respiration 22. Pinna and corneal reflexes very brisk. Acoustic reflex good. Touching the face produces twitching of facial muscles, and even a slight movement of air across the face produces the twitching of muscles and shaking of the head. If animal is stimulated by twisting the ear curious walking movements occur, most marked in hind limbs, and sometimes accompanied by a curious crying sound.

Twenty-third day. Had caught fore-paw in thermo-regulator and had broken it. Animal found dead and temperature of bath 41° C. Death no doubt due to hyperpyrexia.

These two examples give a fairly good general impression of the results usually obtained, though there can be no doubt that the first of these showed some symptoms of raised intracranial pressure secondary to hæmorrhage and infection throughout its time of survival; it is probable that raised intracranial pressure caused absence of function of nervous centres close to the section, thus accounting for the sluggish reflexes and the relative simplicity of the reactions in the late stages compared with those shown by many animals.

(*b*) *Posture.*

The decerebrate rigidity remains as a general rule during the whole time the preparation survives, but after the first four or five days this position is less constant, and may alternate with others in which flexion, either flaccid or rigid, is conspicuous. At this later stage the variability of the positions assumed is noticeable, and it seems probable that the temporary disappearance of the rigidity is due to the assumption of other reflex positions. The maintenance of good rigidity over a long period, as in animal I, certainly makes it possible to exclude it being due to stimulation of cut nerve fibres, since these had undergone degeneration in this animal, and there is, therefore, good confirmation of the generally accepted view of the reflex origin of this position.

The rigidity shows variations according to the position of the animal, and to some extent these variations correspond with those described by Magnus and Kleijn and their co-workers [3], [26], [27], [28], [36], [37], [38], [39], [40], [61], but in the few animals that we have examined carefully we have been unable to get such consistent results as these authors have described. As in our animals the spinal cord has not been divided, the rigidity of the fore limbs is influenced by the position of the hind limbs, so that less constancy must be expected. In

general with the animal lying on one side all four limbs are held rigidly extended, but both the upper fore and hind limbs are relatively flaccid when compared with the lower. This difference is still observed if the animal is suspended in the air by holding it up by its skin while maintaining it in a similar position, but the difference in rigidity is less noticeable than it is when the animal is also receiving pressure stimuli by resting on the table. This contrast between the upper limbs and those resting on the table was very constant and was noticed in a large percentage of the animals, but even in this respect preparations are found in which this difference is scarcely noticeable, or in which the rigidity is asymmetrical so that the contrast cannot be observed. This asymmetry is especially apt to occur in the later stages when a position of general extension of the limbs is much less constant.

During the first few days the position usually assumed by a preparation lying on its side is that described already in the case of animal II on the ninth day, the position of the hind limbs being variable, though most commonly the upper hind limb was also held rather forwards and the lower farther back. On turning the animal over the limbs move, so that the same posture is assumed in the new position. This again is not regular; thus, for instance, in one of the earliest of these experiments, an animal (decerebrated June, 1914) maintained this posture constantly on whichever side it was lying, except on the second and seventh (the last) days, when the relative position of the limbs was the reverse of this, the lower fore limb being held forwards and the upper fore limb backwards. That this was a definite posture was demonstrated on turning the animal; then the limbs were moved so that this atypical posture was adopted also when lying on the other side. Such an atypical posture has sometimes been maintained by other preparations and has then been the usual position for that animal.

Rigid flexed positions may be assumed in an acute preparation, but under these conditions it is rare, and we have never been able to produce them, except accidentally; in the chronic preparations they are a comparatively common occurrence, and indeed some degree of flexion is usually found in one or more of the limbs after the first five to ten days, and, though it may alternate with extension, yet flexion may sometimes be the more constantly maintained posture. The most common of these flexed positions is a rigid semi-flexion of the fore limbs, or of one fore limb, with an acute rigid flexion of the ankle joints and extrusion of the claws of the fore limbs. The position is then one

similar to that assumed by a cat when holding a mouse in its claws or when climbing up a pole. An example of this will be seen in the case of animal VIII, of which a detailed description will be given later. A few other instances may be brought forward.

Animal III.—Large male. After operation had rigidity of average intensity present in all four limbs; the rigidity was fairly symmetrical, though the head was held turned to the left. On the third day this rigidity became less noticeable and when turned the animal tended to curl up and flex the fore limbs. On the fourth day after turning, the previous degree of rigidity had returned, and was maintained on the fifth day. On the sixth day there was a rigid flexion of the ankle joint of the upper fore limb, on whichever side it was lying, with extrusion of the claws of this limb. On introducing a thermometer into the rectum both fore limbs were flexed with acute flexion of both ankle joints and extrusion of the claws, while several extensor thrusts were made with the hind limbs. In this animal the section passed through the anterior end of the right superior colliculus and through the middle of the left superior colliculus, to emerge ventrally 3 mm. in front of the pons at the level of the stalk of the pituitary, but no microscopical examination was made. This animal also gave pseudaffective reflexes and will be referred to again later in this connection; the decerebration was by the older method in which all the brain above the section was removed so that there was no possibility of any connection with higher centres.

Animal IV.—Adult female. Post-mortem, see p. 250. Decerebrated by the later method, the rigidity was only moderate on the first day, but increased on the second, though still below the average; on the third day the animal kicked a good deal during turning, and then assumed a position of rigid flexion of the back and hind limbs with some flexion of fore limbs. On the fourth day there was an average rigidity in an extensor position, but flexion postures were assumed temporarily, during turning, &c., but were maintained only a few minutes, then gradually changing to an extensor posture. On the sixth day the animal was taken out and dried for examination in greater detail. On taking it out of the bath it went into a position of extreme extensor rigidity with retraction of the head. During drying with a towel it made many movements, kicking, withdrawing a limb that was being dried and shaking it, especially the left hind limb. It also made some progression movements. In between these movements positions either of rigid flexion or of rigid extension were assumed.

In the rigid flexed position the ankle joints of the fore limbs were acutely flexed and the claws extended. Unfortunately this animal vomited and choked during drying, so that no further examination was possible.

A position of flaccid flexion was also not uncommon in the later stages. An instance of this is described below.

Animal V.—Half-grown male. Post-mortem, see p. 250. Decerebrated by the later method. Three hours after operation showed little rigidity but made walking movements most of the time. For the first nine hours the animal was kept in an incubator but developed little rigidity; it was then put into a bath and on the next day the limbs had good extensor tone. On the third day there was little or no rigidity. On the fourth day rigidity was absent in the morning, the limbs being quite flaccid, but quite good rigidity developed on turning it to the other side. On the fifth day the rigidity was moderate and on the sixth it had again disappeared, though the pinna and other reflexes were good. The animal was then dried. On washing in alcohol and drying with a towel there were good movements of retraction with a shake of the paw of the limb being dried, especially in the fore limbs, and good extensor rigidity returned temporarily. When dry the animal appeared completely flaccid, with good pinna reflexes, shaking of the head on blowing in the ear, and retraction and shake of each limb on pinching. It was then given to Professor Sherrington for use in his experiments. As soon as dissection was started, kicking movements of all four limbs with movements of the head and neck were made, the animal micturated and then the preparation went into a posture of extreme extensor rigidity with considerable retraction of the head which it then maintained. Following this the extension became gradually less intense, though never disappearing entirely within at any rate twenty minutes, and was renewed in full intensity as soon as the preparation received further stimulation.

Other preparations were sometimes flexed and perhaps flaccid as they lay in the bath, but went into extensor rigidity immediately any examination was attempted. In one or two cases this passage from a flexed to an extended posture seemed to be induced by mere auditory stimuli, but no instance of this was seen in which the evidence was absolutely conclusive, owing to the difficulty of observing the animals while in a bath. It is conceivable that the flaccid flexion is a posture which has some relationship to the sleeping of a normal animal, but no proof of this is available.

Of the animals so far described two (animals II and III) have been distinguished by a tendency to turn their head to the left. This was a common occurrence, being noticed in fourteen animals as compared with nine that turned their heads to the right. This may have been due to the fact that the trephine opening was made on the left side and in consequence the section was generally a little oblique, and nearly always with the tendency to the removal of more on the left side. In thirteen of the above fourteen cases with head held to the left more brain matter was removed on the left side than on the right. On the other hand, of the nine preparations (see cats VI, VIII, XV,

XXII, XXIV), in which the head was held turned to the right, in four the section appeared to be evenly transverse, in four the section had the usual obliquity (more being removed on the left), but the turning of the head to the right was observed in spite of this; the level of the section was not determined in the ninth. The relationship is evidently complex, since the section had the usual obliquity in other cases without there being any asymmetry in the head position; undoubtedly during the first few hours stimulation may play a part.

In the one animal with more brain-stem removed on the right, which turned its head to the left, the position assumed may well have been due to stimulation, since it occurred during the first day, after which the animal died. Stimulation immediately after operation would also account for three out of the four cases in which turning the head to the right was noticed, although the section had removed more brain on the left side, since in these again the turning of the head was only noticed during the first day. In the animals with an apparently square section, in which the head was turned to the right, this posture was not marked except in one case. In all cases where there was an asymmetrical head position the level of the section was relatively anterior, and some few cells of the red nucleus were probably left intact and may have been functioning on one side at least. In fact, this whole turning of the head to the side most damaged might be explained if the tone of the muscles of the neck was increased by a crossed connection with a centre lying at about the level of the section, and it is possible that the lowermost cells of the red nucleus may function in this way.

Of the thirteen animals showing a persistent turning of the head to the left, one (XXVI) has been shown histologically to have had more of the red nucleus remaining on the right side than on the left, and in all the others the section was sufficiently high for a part of the red nucleus to remain, with the possible exception of two. The most difficult case to explain is that of animal VI (for post-mortem see p. 249) in which histological examination showed an almost complete destruction of the left red nucleus, the right red nucleus being partly present though showing some chromatolysis. Yet this animal gave auditory reflexes with movement of the head to the right during the two days it survived. Unless the hæmorrhage had interfered with the tract from the right red nucleus, the above hypothesis would seem untenable, and it cannot be regarded as established at present; further the posture is not

easily correlated with results of stimulation of the mid-brain reported by Graham Brown [8].

Many of the animals had sufficient rigidity to stand if propped into position, as described by Sherrington in the acute preparation, and most of them were able to maintain a very natural sitting posture. This consisted in making the animal lie on one side and propping up the body on the two elbows, so that the head was held in an erect position. Many could sit in this position on either side and maintain it for a considerable time, though usually after about five minutes the head would gradually drop, being allowed to fall sideways, and the preparation would lie down, the head in this procedure being carefully lowered so that no sudden impact with the table occurred. Similarly, the head was gently lowered if the animal was pushed over out of its sitting position. If the animal spontaneously held its head to one side, it was often only possible for it to balance itself in this sitting posture when lying on the flank opposite to the side to which the head was turned. All the postures assumed are more or less comparable with some seen in normal cats, the flexed positions that are often assumed in the later stages resembling those of cats curled up asleep.

(c) *Magnus Reflexes.*

These have been carefully investigated in two animals only owing to the difficulties with animals kept in a bath, though a few data resembling his results have been obtained on one or two other animals,

Animal VII.—Male, three-quarters grown. Post-mortem, see p. 251. Decerebrated by the later method. On examination twenty-seven hours after operation the animal could sit on either side and had good rigidity of all four limbs when standing, sitting, or lying on its right side. The rigidity of the fore limbs was less than that of the hind and was almost completely absent when the animal lay on its left side. In the standing position little change in rigidity was noticed as the result of raising or lowering head, and when lying on its back there was scarcely any rigidity in the fore limbs in any position of the head. When lying on right side bending the head down to the right increased the tone in the two hind limbs, and rotation of the head (jaw upwards) caused increased tone in the left fore and hind limbs and a slight decrease in the right hind limb, with no perceptible change in the right fore; the opposite changes occurred on turning or rotating the head in the opposite direction. Lying on the left side bending the head up to the right increased the tone in the right hind, but no other change was distinguishable, and rotation (jaw upwards) also increased the tone in the right hind, slightly increased that in the right fore, and slightly decreased that in the left hind; the opposite effects were obtained by the reverse movements.

Animal VIII.—Female. Post-mortem examination, see p. 252, and for more detailed description of the animal see p. 208. Decerebrated by the later method. Examined on the seventh day. When lying on its back reflexes orthodox, showing flexion of the fore-limbs when the head was bent right forward, maximum rigidity with head in -45° or $+30^{\circ}$ position, this decreasing a little as the head was moved to 0°. This animal had little rigidity in the standing position and could not be made to stand. Placed on one side it assumed always a definite posture on whichever side it was lying; in this the lower fore was completely extended, the lower hind three-quarters extended, the upper hind semi-flexed and the upper fore was flexed and carried forward over the other, and the position of all the limbs was a rigid one. On flexion of the terminal joint of the upper fore there was extrusion of the claws. While lying on the left side bending head to the right caused extension of all limbs except that no change was noticed in the right fore; when on the right side there was extension of both fore-limbs and slight flexion of both hind on bending the head to the left. Lying on the left side, rotation of the jaw upwards caused extension of both hind-limbs and no perceptible change in the fore-limbs; on the right side rotation of the jaw upwards caused flexion of left hind and right fore, and extension of left fore, but no change in right hind. Movements of the head in the opposite directions in every case reversed the changes in the limbs, with the exception that rotating the head (jaw downwards) when the animal was lying on its right side not only reversed the changes in rigidity described for the opposite movement, but also caused a movement forward of the left fore-limb. In this cat the rigidity was slightly asymmetrical, since the preparation could sit on either side, but did so more evenly and securely if resting on its left flank, and it showed some tendency for the head to turn to the right. Some such asymmetry may account for the atypical reactions to these tests. The preparation died soon after the examination, apparently owing to a secondary hæmorrhage at the base of the brain.

(*d*) *Opisthotonos.*

This is not uncommon immediately after operation; in these animals the respiration rate is usually slow (though sometimes there is a fast and shallow respiration), and the condition is generally accompanied by tonic fits in which the rigidity undergoes extreme accentuation. In fact this head position was never seen except accompanying extreme extensor rigidity and merely appeared to be the result of such extreme rigidity. A few instances may be described.

Animal IX.—Old male. Post-mortem, see p. 247. Decerebrated (earlier method) 3.30 to 4.30 p.m. At 5.30 p.m. put into bath. Extreme rigidity, especially of hind-limbs.

Head retraction but not extreme. On second day reflexes brisk. Extreme rigidity of all four limbs. Lifts head to left to acoustic stimuli, but no

opisthotonos now seen. On ninth day extensor rigidity still good, having remained very marked since operation, but auditory reflex has almost disappeared since fifth day. Head retraction now again present. The rigidity of the hind-limbs is, however, definitely less than before, the fore-limbs are fairly rigidly extended except for a rigid flexion of the ankle joint with extension of the claws like that described in cat II. In the evening showed marked rigidity of mastication muscles with some clonus of the jaw on opening the mouth. Some nystagmus of eyes with rapid movement to the right, especially seen in the right eye. On the eleventh day found dead, and evidence found of old hæmatoma with later infection.

Animal X.—Decerebration (earlier method) 2.45 to 4.15 p.m. Considerable hæmorrhage. At 9 p.m. in incubator, rectal temperature 41·2°, respiration rate 24, rather irregular, and each inspiration accompanied by slight spasm of muscles of back. Rigidity intense and whenever the animal is touched it goes into extreme opisthotonos. At 10.45 p.m., temperature 38·8°, respiration rate still 24, with long inspiratory pause and only occasional spasm of back muscles. Attacks of opisthotonos as before. This opisthotonos was brought on most easily by touching the nose; it could be made to relax generally, but not always, by flexing the head, and would itself relax spontaneously to some extent after a time. On one occasion insertion of a thermometer into the rectum produced a strong defæcation reflex with immediate relaxation of the intense rigidity and disappearance of the opisthotonos.

On the following morning the opisthotonos had disappeared, breathing was more regular, 20 per minute, with a rectal temperature of 37·8°. Rigidity marked but not so intense, and twitching movements of all four paws present, these occurring with each inspiratory movement. On the third day respiration normal, muscle spasms no longer seen, and the animal made an inco-ordinated mew twice when taken out of the incubator. Animal died at the end of the day and post-mortem showed a considerable hæmatoma at the base of the skull. No detailed examination of the level of the section.

Animal XI.—Female, half-grown kitten. Decerebration (later method) 2.30 to 3.15 p.m. Signs of reactionary hæmorrhage immediately after operation with considerable oozing from the wound. Attacks of marked rigidity and head retraction. Found dead next morning. On autopsy considerable hæmatoma; the section extended from in front of superior colliculi to about 0·5 millimetres behind the anterior end of the pons.

It will be clear from these examples that this condition is seen in animals with evidence of post-operative hæmorrhage, and generally blood is also found below the tentorium. Death in the first twenty-four hours is common, but if the animal survives the opisthotonos disappears, and does not reappear again except in the case of an infection of the base of the skull such as was the case in animal IX. The exaggeration of the position as the result of some sensory stimuli, and

its inhibition by other stimuli, is also another noticeable feature. In some animals auditory stimuli or a jar such as that from shutting the incubator door seems to have been sufficient to induce a head retraction spasm.

Head retraction of less intensity may occur in animals with a normal degree of rigidity if this be exaggerated temporarily by nervous stimuli such as the dissection of a nerve. An example of this was seen in animal V, which has already been described. Reflex factors, as well as conditions with raised intracranial tension, must therefore also play an important part, and this condition is merely an exaggerated extensor rigidity.

While a hæmatoma and usually subtentorial hæmorrhage have been found in all such cases, many other animals may show quite similar hæmorrhage on autopsy and yet have never presented these symptoms. The cause of opisthotonos cannot be hæmorrhage into the fourth ventricle, since it has been observed in animals in which no such hæmorrhage was found.

(*e*) *Temperature Regulation.*

There seems to be no doubt that after operation these preparations have no power of temperature control whatever, and that they never regain it however long they may survive the operation. If they are kept in an incubator the setting of the incubator temperature has to be exactly right, so that the heat loss balances the heat production, in order to maintain a constant temperature, and the setting of the incubator required for different animals is not the same. Even for the same animal the balance has to be hit exactly, taking into account the degree of the dryness or dampness of the fur, and to strike such a balance becomes a difficult problem even if the air be maintained saturated with moisture.

Not only are they unable to adapt themselves to even small changes in temperature but they have never shown normal reactions to these temperature changes. If their body temperature is dropped suddenly no shivering has ever been observed, nor does their respiratory rate increase to a normal extent if their body temperature is quickly raised. It is true that few people have seen a normal cat shiver in cold weather or pant under the influence of heat, but anyone who has tried washing a cat will have observed the shiver (see also animal V), and if a wet cat be dried under sufficiently warm conditions the respiratory rate may easily rise to 70 or 80 a minute. The ordinary cat does not

usually show either symptom, since it is careful to keep itself under comfortable conditions and has a thorough insulation in its fur. The metabolism of these preparations has not so far been investigated by us, but we have no reason to doubt the low metabolism figures obtained on the acute preparation by Roaf [47], since the difficulty of keeping the preparations warm has always been remarkable. The stretching out of the limbs in extension no doubt increases the heat loss, but even so it is surprising that keeping the animals on a warmed operation table, surrounding them with hot-water bottles and covering with a blanket, is usually only just able to keep the animal's temperature normal if the room is at all cold, i.e., 15° C. There is also some evidence that the metabolism is greater the higher the temperature and that it decreases with a fall in temperature, so that there is no effort at a control of body temperature through a control of metabolism. Thus in an incubator animal with its fur greased and in an atmosphere saturated with moisture (when the loss of heat is accomplished by radiation and conduction), the difference in temperature between the animal and the incubator is usually greater the higher the temperatures happen to be. Thus with a high rectal temperature a difference of 5° C. above the temperature of the incubator may be found, and with a low rectal temperature the difference between the two may be only 3° C. Thus there is a tendency for the rectal temperature to swing more widely than that of the incubator. The resulting difficulty in finding a correct setting for the incubator is readily seen by reference to a few examples.

The general correspondence between the animal's temperature and that of the incubator is well shown in fig. 1, which represents the temperatures observed in cat VII, of which some description has already been given. This animal was kept immediately after operation in an incubator in which the air was constantly saturated with moisture by having the wall covered with damped cloth. Considerable difficulty was found in getting a correct setting of the incubator and it is seen that between eight hours and twelve and a half hours on the first day the rectal temperature of the preparation dropped 2·1° C. (from 37·2° to 35·1° C.), corresponding with a fall of 1·5° C. in that of the incubator. It is also noticeable that after three and a half hours on the first afternoon the rectal temperature was 39° C. and was rising rapidly as the result of an incubator temperature of 29·7° C. dry and 29° C. wet bulb, while twenty-seven hours after operation the rectal temperature was fairly steady at only 36·2° C., though the incubator setting had now been adjusted to give a temperature of 30·3° C. dry and 29·8° C. wet bulb. The

difference in the two results is probably due to the gradual loss of the insulating action of the fur as the effect of the penetration of the moisture through it. This was demonstrated accidentally on the second afternoon. At 3.10 p.m. the animal was taken out of the incubator and was examined for Magnus reflexes in front of a gas stove until 4.25 p.m. During this examination its rectal temperature rose to 39·7° C., its fur became dry and in good condition, and it was then returned to the incubator in the belief that its temperature would gradually drop again to 36·2° C., since the incubator setting had not been altered. The

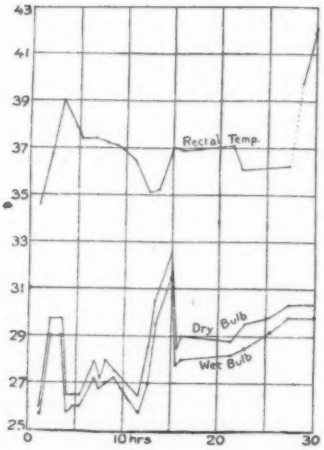

FIG. 1.—Experiment VII. Abscissa: Time in hours from end of operation. Ordinate: Temperature degrees centigrade. Lowest curve: Wet bulb temperature of incubator. Middle curve: Dry bulb temperature of incubator. Upper curve: Rectal temperature of animal. Dotted part of curve: Change when animal was out of incubator being examined in front of a gas stove.

observer was interrupted by teaching work and when the animal was again examined, one hour and thirty-five minutes later, it was found to be dead, with a post-mortem rectal temperature of 42·1° C. This case, therefore, illustrates very well the difficulties of incubator preservation of these preparations, and the numerous factors that have to be taken into consideration, as well as demonstrating the absence of any control.

The same points, and also the general course of such an incubator experiment, may be seen in the case of cat VIII (also previously described in relation to the Magnus reflexes). The general history of its temperature changes is illustrated in fig. 2; but a more or less detailed account may also be given to serve as an example of an incubator experiment.

Animal VIII.—Female. (For post-mortem see p. 252, and previous description p. 203). Decerebrated by later method so as to preserve stalk of pituitary. Rather ragged section and considerable hæmorrhage afterwards. Large piece of gauze left in, but in spite of this a considerable hæmatoma formed shortly after the end of the operation. Placed in steam-heated incubator at 30·8° dry and 30° C. wet, i.e., about temperature at which cat VII had a rapid rise of temperature on its first day. At three and a quarter hours the rectal temperature was still below 35° C.; at four and a quarter hours it was still only 34° C., though the incubator temperature had been still further raised. The incubator was then set to give 33·5° dry and 32·8° wet bulb, and the rectal temperature gradually rose to reach 38° C. after about nine hours. The

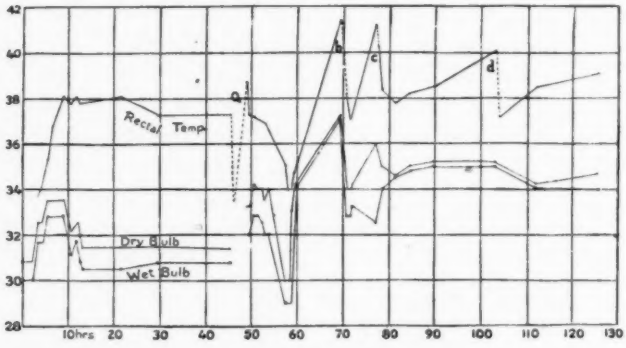

FIG. 2.—Experiment VIII. Abscissa: Time in hours from end of operation. Ordinate: Temperature. Lowest curve: Wet bulb temperature of incubator. Middle curve: Dry bulb temperature of incubator. Top curve: Rectal temperature of animal. Dotted parts of curve: Animal out of incubator—(*a*) taken out, wound dressed; as bodily temperature fell fur treated with paraffin and animal then warmed in front of gas stove; (*b*) and (*c*) cooled by being kept in a room for a short while; (*d*) examined in front of stove for Magnus reflexes.

incubator temperature was then gradually reduced and regulated to give a temperature of about 31·5° dry and 30·5° wet bulb, when the rectal temperature reached a steady level at about 37·3° C. During this time the animal had had good rigidity of all limbs; twelve hours after operation it showed brisk corneal and pinna reflexes, and some mastication reflex, and when the ear was twisted it moved its head and fore limbs slightly and showed a definite increase in decerebrate rigidity.

Thirty hours after operation reflexes as before but mastication no longer seen; respiration rate 21, temperature 37·3° C. Lying on right side it now had good rigidity of all four limbs, but on turning on to left side showed some flexion of back, good rigidity of hind limbs, little rigidity in the left fore, and it held the right fore rigid, but flexed and placed forward across the left, with the ankle joint acutely flexed and the claws extended. It kept its head turned to

the right if put into a sitting posture. The tail was intensely rigid, and was wagged whenever the animal was touched.

Forty-six hours after operation taken out of incubator, and gauze plug removed from wound; hæmatoma found infected. Animal kept on warmed table but room temperature only 9° C. (owing to post-war conditions), and the rectal temperature soon dropped to below 35° C. Animal then warmed in front of gas stove and lubricating oil rubbed into fur to diminish its heat insulation value.

Returned to incubator at 2 p.m. (i.e., fifty hours after operation) with temperature of 38·7° C. The respiration rate was then 20, having dropped to 15 per minute when the body temperature was at its lowest. Fig. 2 shows the changes in temperature occurring after this and the close correspondence between the rectal and incubator temperatures. When the rectal temperature had risen to 41·6° C. the respiratory rate was 40, dropping again to a rate of 31 when the rectal temperature had reached 38·1° C. on taking the animal out of the incubator and keeping in a cold room. This drop of temperature occurred in about thirty-eight minutes, and yet there was never any sign of shivering. The posture of the animal when lying on the left and right sides was as before. The wound was opened up and some pus evacuated.

Sixty-six hours after operation the animal was again examined. It now had good extensor rigidity of all four limbs when lying on the *left* side, and on being turned to the *right* side there was good rigidity of the hind limbs and extrusion of claws, and on stimulating by twisting the ear the fore limbs assumed a rigid flexed position with extrusion of the claws, and maintained it.

One hundred and three hours after operation the rectal temperature was 38·5° C., and the respiratory rate 32. The upper fore limb was kept flexed on whichever side it was lying. On touching the animal there was reflex extrusion of claws and either retraction or prodding forward of the limbs.

One hundred and eighteen hours after operation the animal was much as above, but when traction was made on its flexed upper fore limb, it withdrew it with a clawing movement. It also made a cry—an inco-ordinated mew—when being turned.

One hundred and twenty-seven hours after operation was as above but on various stimuli, such as mere touching, would often extend a limb and spread out claws, in the position a cat holds its limbs when stretching after waking up.

At the end of the sixth day the position of the animal on whichever side it was lying was very definite and has already been described in connection with the Magnus reflexes. It had no auditory reflexes, but by this time some mastication had again returned. The respiration rate was 33 with a rectal temperature of 39·1° C. There was a discharge of pus and wax with disintegrating hæmatoma from the wound, and in the middle of the seventh day the animal died as the result of a secondary hæmorrhage within the cranium. Urine passed during the third day contained no trace of sugar.

The effect of body temperature on the respiratory rate is also well shown in the case of cat XII kept in an incubator with a wet bulb control, but in which the air was not saturated with moisture and where the insulating action of the fur was not interfered with. The changes in body temperature and of the incubator for thirty hours, starting seven hours after the end of the operation, are shown in fig. 3; the wet and dry bulb readings were taken at frequent intervals and the rectal temperatures were taken with an electrical resistance thermometer and were recorded every minute on a Gamgee [16] thread recorder as

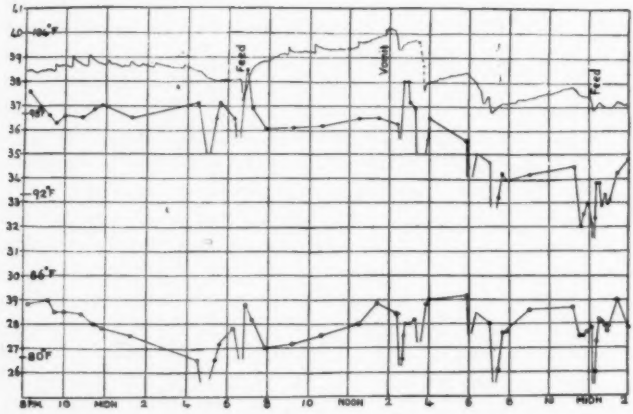

FIG. 3.—Experiment XII. Abscissa: Time: operation finished seven hours previous to commencement of record. Ordinate: Temperature. Lower curve: Wet bulb temperature of incubator. Middle curve: Dry bulb temperature of incubator. Upper curve: Rectal temperature of animal (record with resistance thermometer). Gaps in records, opening of incubator door.

described by Woodhead and Varrier Jones [65]. In all, more than forty-five observations of the respiratory rate at varying body temperatures were made on this animal, though the results were somewhat modified by the gradual development of mucus in the trachea giving some irregularity in the respiration with a later development of lung congestion. If all the figures for the respiratory rate during the first few days are averaged the following results are obtained:—

Temperature	Number of observations	Average rate per minute
36° to 37°	4	23
37° to 38°	18	28
38° to 39°	16	33
39° to 40·1°	7	36

If, however, only the earlier figures are taken, before much tracheitis had occurred, the respiratory rates are rather slower but the relative differences are much the same.

Average temperature	Number of observations	Average rate per minute
36·1°	1	15
37·2°	4	19
37·8°	5	25
38·0°	2	29
38·3°	4	31
38·7°	4	32
39·5°	3	33

The brain section in this animal was from the anterior end of the inferior colliculi to 1 mm. in front of the pons, but a detailed histological examination was not made. It will be noticed that in this

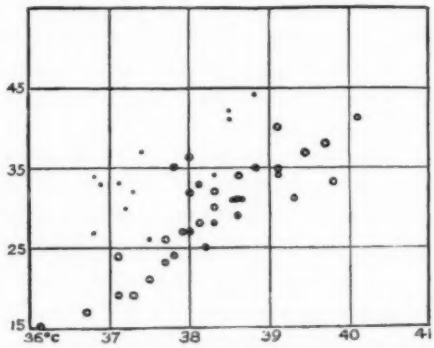

FIG. 4.—Experiment XII. Abscissa: Rectal temperature. Ordinate: Respiratory rate per minute. Variations in respiratory rate with changes in temperature. o = Observations during first twenty-nine hours. . = Observations made later than this.

animal as well as in cat VII there was a very definite dependence of the respiratory rate on the body temperature. This is still more clearly seen in fig. 4 in which the respiratory rate observations are plotted against the body temperatures. The figures are obviously affected by other factors, such as the mucus already referred to, and quite possibly the respiratory rate is different for any given temperature, if the temperature is then falling, compared to what it would be if the temperature were rising. In spite of these variable factors it is clear from a consideration of these two examples that there is a relationship, and that the temperature coefficient is rather high, probably about 4·0, possibly as high as 5. But in any case the effect is much less than in the normal cat where a slight rise in body temperature may easily

give a respiratory rate of 80 [20] [30] [48]. That the temperature coefficient is so high may be partly due to the fact that not only might the change in temperature affect the respiratory centre directly, but it might also do so indirectly through altering the metabolism.

In only one instance was a really fast respiration seen with a raised body temperature. In this animal the temperature rose to 42·8° C. in an incubator through an accident. At the time of observation it was moribund and its respiratory rate was about 60, but this animal had had a considerable reactionary hæmorrhage, with marked opisthotonos and convulsive spasms, and its fast respiratory rate may have been due to other factors. In any case the rate observed is not very different from what might be expected at this body temperature, judging by the other animals. The section in this animal was also rather anterior and very ragged.

With regard to the respiration it should be noted that as a rule with a normal body temperature the respiratory rate was about 24 per minute, which is about the normal rate for a cat. Irregular and spasmodic breathing described by Macleod [34] [35] as occurring spontaneously in some animals after decerebration was not seen except where there was fairly definite evidence of hæmorrhage, as in cat X, nor can we agree with the provisional statement made by Macleod that "when the posterior corpora quadrigemina are even slightly wounded spontaneous respiration is seldom, if ever, observed." We have repeatedly made sections through this level and observed normal respirations, and we have even made sections through the very posterior edge of the inferior colliculi without having trouble with the respiration (e.g., cat XXI described later, survived over twenty-two days with a normal respiratory rate, and cats XX and XXIII furnished other examples of this). The contrast between our experience and that of Dr. Macleod may depend on the fact that our animals immediately after the operation were left quite quiet without further experimentation, while such a course is impossible in dealing with the acute preparation. Any manipulation or stimulus must increase the risk of reactionary hæmorrhage either below the tentorium or into the substance of the medulla, and that this was a common occurrence even in our animals may be seen by reference to the anatomical descriptions. Clearly the macroscopical inspection of the brain-stem does not allow the physiological level of the decerebration to be determined, and consequently discrepancies between different observers are to be expected according to the relative probability of post-operative hæmorrhage. A similar

explanation may well account for the discrepancies between Trevan [58] and ourselves as to the effect on the respiratory rate of section at various levels.

Fig. 3 demonstrates well how sensitive the body temperature was to the changes in the incubator produced by opening the door for a few minutes, as for instance for feeding.

That the wet bulb temperature is very important is shown by the fact that animal VII required a wet bulb temperature of about 29° C. with a dry bulb reading of about 30° to maintain a normal temperature, while animal XII required a wet bulb temperature of between 28° and 29° with a dry bulb of about 34° for the same result. And yet it was not the only factor; the rectal temperature showed a rise in cat XII between 8 a.m. and 2 p.m. with a rise in the wet bulb temperature, but it also showed a fall between 4 p.m. and 10 p.m. although the incubator wet bulb temperature had altered very little, while the dry bulb fell considerably. Also the difference seen between animals VII and VIII, one requiring a wet bulb temperature of 29° and the other of 31° (before the fur was greased) with almost complete saturation with moisture, to maintain normal conditions, requires explanation. Cat VII had an excellent coat and cat VIII was rather mangy, and this may well have been the cause.

The incubator temperatures in the case of cat XII were rather variable; the reason for this was that the outer door of the incubator was left open throughout the experiment to allow the repeated examinations of the respiratory rate on this animal, and the glass door did not give adequate insulation. The sudden peaks occurring in the rectal temperature record in this figure are also of interest. They were always seen when an animal attempted to defæcate against the resistance of the thermometer; since they show fairly steep falls directly the efforts ceased they may represent a change in temperature which was chiefly local.

The absence of shivering on cooling was specially tested in one animal (cat XIII) four hours after operation. This animal's reflexes were brisk and the section was an anterior one passing through the superior colliculi to 2 mm. in front of the pons; it was operated on by the older method. Though its temperature was reduced from 39·5° to 37·8° by wetting with cold water (the normal temperature for a cat is about 38·5°) within five minutes, yet no sign of shivering was seen. In another animal which has already been referred to (cat V) the preparation was kept in an incubator for the first nine hours; it was con-

stantly making running movements, so that it was not found easy to balance the heat exchange. At the end of this nine-hour period its rectal temperature was 40·9° C.; then it was cooled down by holding under a tap delivering water at 16·5° C., the water being rubbed into the flanks, so that the temperature fell to 37·8° within sixteen minutes, and yet no sign of shivering could be observed. That shivering does not occur either even in animals that have survived much longer is clear in that no such movement was ever seen in animals, such as cat II which was taken from a bath and had its temperature dropped rapidly from a normal level to one much below normal during the process of drying.

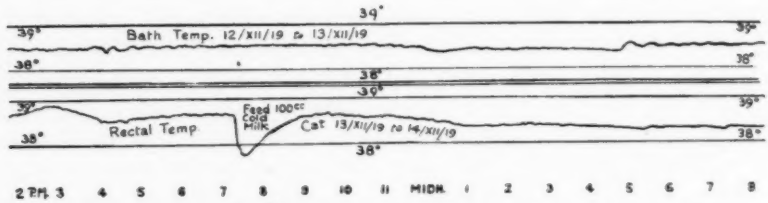

FIG. 5.—Experiment XIV. Abscissa: Time. Ordinate: Temperature. Lower curve: Rectal temperature of animal in bath, December 13 to 14. Upper curve: Temperature record of bath December 12 to 13.

Fig. 5 gives examples of records with a resistance thermometer of the rectal temperature of animal XIV (described a little later) kept in a water bath, as well as a record of the bath itself, the two records being taken on successive days, and the part reproduced includes the early morning hours when the greatest fluctuations of the bath temperature usually took place. The relative steadiness of the rectal temperature by the use of this method is very noticeable, and also the rapid drop of nearly 1° C. in the rectal temperature on feeding this animal (of 2·1 kilo weight) with about 90 c.c. of cold milk by stomach tube. The effect of feeding was always marked, if the food were cold, so that in incubator experiments it was necessary first to warm the milk to the body temperature, since under these conditions recovery of a normal temperature took place much more slowly.

(*f*) *Pseudaffective Reflexes; Mastication and Vocalization.*

Pseudaffective reflexes have already been described by Woodworth and Sherrington [66] in acute preparations, and all those that they have described may be observed in the chronic animal, as well as others which are rarely seen except after survival for a few days. The most

common of these reflexes is the lashing of the tail when the animal is touched or stimulated, as by twisting the ear; this reflex is seen in a large percentage of the preparations (both acute and chronic), e.g., cat VIII. Kicking movements and running reflexes may also be induced often by touching an animal, as happened for instance in animals II, IV and V. All these reflexes may be seen in the acute preparation, but they become more common as an animal is kept, and may often be present after the fourth day when the animal has been entirely passive during the first few days. The kicking movements are usually more widespread and general in the later stages than in the earlier, and while they are relatively difficult to induce in the first few days except by strong stimulation of some area on the head, in the later stages mere touch stimuli at any situation will often produce a reaction. Some instances of these may be briefly described.

Animal XIV.—Female. Decerebrated by earlier technique. Had good rigidity with head held to the left, brisk pinna and conjunctival reflexes, pricking of the left ear to auditory stimuli, and it swallowed a stomach tube with a passive reflex action on the first day. By the fourth day the head was raised to the left when sounds were made, especially to such noises as shuffling the feet on the floor, and the stomach tube was only swallowed after apparent objection. This consisted in bending the head backwards, biting, attempts at spitting out the tube and general movements of the head which suggested an attempt to get rid of the tube. The eyes had been washed out with water every day, and on this day it began to "object" to this process, squirming its head backwards and making the washing difficult. On the fifth day there was some conjunctivitis of the left eye and the washing of the eyes was also accompanied by movements of the legs. The section passed just in front of inferior colliculi dorsally to about 3 mm. in front of the pons ventrally. No detailed examination was made.

Animal XV.—Male. Decerebrated by later method. Rigidity good and reflexes good. Slight movements of progression in left hind limb on first day. On second day some progression movements, though slight, in all four limbs from time to time. Stomach tube swallowed passively. No auditory reflex.

On third day on turning the cat over, it had a flexion spasm of both fore paws associated with an increased rate of respiration and some turning of the head to the right.

On fourth day some chewing of the stomach tube but no "objection" to it. A slight nose-licking reflex present after feeding.

On fifth day there was some conjunctivitis. On cleansing the eyes there was apparent objection, movement away of the head and bringing forward of the fore paws as though to push the hand away, but this was badly co-ordinated and ineffective. The condition remained much the same till the eighth day,

when the animal "jumped" and showed increase of rigidity on cleansing the eyes but no longer moved the fore limbs. It died from a septic enteritis and pneumonia at the end of the eighth day. The level of the section was symmetrical and passed between the colliculi dorsally to the anterior edge of the pons.

These animals illustrate the gradual change during the first few days with the appearance of reactions not seen at first. Ophthalmia was a common occurrence (due no doubt to their blindness); the apparent objection to the cleansing of the eyes was never seen in the first few days, but was nearly always seen after the fourth or fifth day. During the first few days after operation, the stomach tube is usually well swallowed but without any effort at mastication, after this there is often developed a more complicated reflex, in which the tube is taken with avidity with a well co-ordinated chewing movement which might be so effective as to puncture a stout rubber catheter. Once the tube had reached the stomach the chewing movements would usually cease, to recur again from time to time. It was often noticed that these chewing movements recurred more commonly at a time when milk was flowing through the tube into the stomach. Whether there was any reflex connection between the stomach distension and the mastication reflex is however doubtful, since at this time mechanical movements of the tube in the mouth were liable to occur. On the removal of the tube in a good animal there would occur a nose and mouth licking reflex, usually continuing for two or three licks. A similar nose licking reflex has been described in dogs by Meltzer and Githens [42], and like them we have found that such a response may sometimes be induced by pinching of the nasal septum, but in our preparations it occurs much more regularly as a part of a mastication complex. This nose licking is also very common, even in animals that do not otherwise show it, just before vomiting occurs, and under these conditions some mastication movements usually accompany it.

The mastication movements were usually well co-ordinated and after a few bites food placed near the back of the mouth was swallowed, but the mastication was never sufficient to bite any solid food into small fragments; if the solid food were placed in the front of the mouth it might remain there without any movement occurring, or it might be spat out, or very occasionally chewing movements might be induced. If a number of pieces of solid food were given to such an animal the reflex soon fatigued (a cat is a slow eater) and the bolus of food was left stationary, even though lying at the back of the throat. If such a pre-

paration was then stimulated, as for instance by a slight tap on the nose, it would shake its head, apparently "wake up" and the bolus was immediately swallowed. A mastication reflex was often induced by merely opening the mouth. The position of the section in animals with simple mastication reflexes may be seen by reference to cats III, IV, VIII, all of which showed this reflex well.

After the fifth or sixth day pseudaffective characteristics often appear in this mastication reflex, the tube being apparently objected to as in animal XIV, though food would be well taken. In this reaction it may kick and bite and make the other movements described in the case of cat XIV, or it may be less definite. The sequence of different types of mastication reflex is usually as above, but there are variations, and in our series of 124 complete decerebrations we have had two which showed this seeming objection even on the first day. This was the case with animal XII already referred to, and also in the case of a kitten of 1·7 kilo weight (cat XVI) in which the section passed between the colliculi to the anterior end of the pons. It will be noticed therefore that in these cases the sections were at a normal level.

In many cases the mouths of the animals were washed with 1 in 60 carbolic for cleansing purposes. This process has also been accompanied by a seeming objection, shaking of the head, movements of the limbs, &c.; this reflex also has not been seen during the first few days.

Though the reflexes so far described seem superficially to have some relationship to emotion, they are clearly, even to a casual observer, merely pseudaffective, since they differ from many spinal reflexes only by being rather more elaborate, and since in such a decerebrate animal they appear with a mechanical precision whenever the animal is put under the same conditions. It is also very noticeable that a preparation that appears to object strongly to having its eyes washed will allow the wound on its head to be picked up roughly with forceps while a stitch is passed or removed, and not a movement of its limbs may occur, though a simple rigid extension is maintained. To the stimulus of a foreign body in the eye it has an habitual reflex response, but the puncture of a needle in the scalp is an abnormal stimulus unconnected with any habit or reflex. We can therefore unhesitatingly confirm Sherrington's interpretation of these phenomena.

A type of pseudaffective reflex very rarely seen except in chronic preparations is vocalization. This was only seen in a small percentage of the animals, occurring in ten out of the series of 124 operated on.

Of these ten animals four purred, and where purring occurred at all it was usually repeated. An example is described below.

Animal XVII.—Male kitten, weight 1·3 kilo. Post-mortem see p. 248. Decerebrated by earlier technique. Reflexes fairly brisk and moderate rigidity on second day. On fourth day purred after feeding. This commenced about five minutes after the end of feeding and would then continue for a considerable time. Purred after each feed till the sixth day. When touched would stretch out claws. Occasionally spontaneous purring occurred in bath. On sixth day head wound suppurating and purring reflex no longer seen. On seventh day reflexes very sluggish, even swallowing reflex being poor. Stomach tube inserted in consequence into trachea and 70 c.c. of milk poured into it. (In the ordinary reflex animal it is practically impossible to put the tube down the trachea owing to the swallowing reflexes.) Considerable dyspnœa after this. When fed again, eight hours later, reflexes still very bad. but on stroking the chin after feeding it commenced to purr, but this only lasted about a minute. On ninth day the wound suppuration was improving and reflexes much more brisk. Purring again after morning feed. On tenth day reflexes very dull, respiratory rate very fast and no purring. Death later in the day from lung abscess and empyema, obviously resulting from the passage of milk into the lung.

Animal XVIII.—Young female, weight 2 kilos. Decerebrated by earlier method. Auditory reflex and purring after food present on first day. Vomited and died of suffocation on first night. Section through anterior part of inferior colliculi.

The occurrence of purring with regularity after feeding was very striking and it could not be induced in any animals in any other way. Possibly on the seventh day in cat XVII the stroking under the chin assisted in the development of the response, but it is unlikely, since this form of stimulus was often tried and never at any other time with success. On the other hand, food in the stomach formed the stimulus for the purring in three out of the four animals; the fourth in which it developed spontaneously will be described in more detail later. The disappearance of the purring after food in cat XVII with the development of suppuration in the wound, its return as the wound condition improved, and its disappearance again with the development of the lung abscess was very noticeable, and is of interest in that the animal was kept in a bath, so that the body temperature remained fairly constant, except that the animal was once taken out and dried in an incubator. Purring was observed with a rectal temperature as high as 39·2° C. in the bath and as low as 36·5° in the incubator, while the temperature during the time that purring was absent was about

39·2°, so that it was not change of temperature that caused the purring to cease. With infection, however, there is evidence of the dulling of this reflex, much as infection will diminish spinal reflexes in man or decrease the appetite. But the condition in these preparations is very different from real appetite, since though the purring occurs after food, no sign of even a pseudaffective response is observed if food is withheld.

Animal XIX.—Young, weight 2 kilos, sex not noted. Decerebrated by earlier technique. After operation had good rigidity, good reflexes, head kept to left. Maintenance of good sitting posture lying on right side. No auditory reflex. One and a half hours after operation put into bath and showed repeated strong movements of head to left resembling a clonic movement. After two and a half hours found in bath clawing at the stirrer, all claws extruded but animal purring. On handling it made violent kicking and running movements, and in this kicking its head fell under water. After this it gave two loud co-ordinated mews—not those of pain so much as those of an angry cat. It was taken out of the bath and wrapped in a towel, when it purred again for a while. It was then put back into the bath, when it had no further movements but commenced to purr again. Reflexes and rigidity good. Slight movements of head to acoustic stimuli now present. Later it commenced kicking movements again, but was hobbled. Sounds appeared to increase the movements. When fed it swallowed the tube normally and no purring was noticed after. The wound was restitched with no reaction by the animal occurring. It died during the night, possibly from hyperpyrexia as the result of violent exercise in the hot bath.

Autopsy showed a slight intracranial hæmorrhage (about the size of a small pea) and the section passing through the anterior half of the superior colliculi to 2 mm. in front of the pons, the section being slightly oblique with rather more removed on the left than on the right. All the nervous tissue above had been completely removed. Histological examination was not possible owing to post-mortem softening.

This animal appeared to have vocalization reflexes occurring immediately after operation in a more or less disorganized form. It will be evident from the three examples quoted that the level of the section has been rather anterior, and it might have been concluded that the reaction depended on centres lying above the level of the pons. But another cat which purred (cat XX) seems to disprove this.

Animal XX.—Female, weight 2 kilos. Decerebrated by earlier technique. Rigidity good. No auditory reflex. Purred after feeding on the third day, and repeated this after all meals until it died at the beginning of the fifth day. Cause of death uncertain, though there was superficial infection of the wound.

The section passed through the lower parts of the inferior colliculi to the upper edge of the pons. No histological examination attempted owing to post-mortem softening of the brain.

It seems to be therefore established that purring reflexes depend on reflexes through centres in the medulla—though such centres are probably high in the medulla, since the reaction is usually not seen for the first few days after operation, and shock is probably more prolonged in the immediate neighbourhood of the section. It is noticeable that purring was only seen in young animals, and then usually in females, all animals which might be expected to purr readily during life, and in which there may have been a purring habit. The possibility of a medulla-initiated habit is strengthened by a consideration of those animals in which vocalization in the form of growling occurred.

Growling was observed in three animals, and shows considerable contrasts when compared with the purring reflexes. All three animals were adult males, and two of them old scarred animals which had evidently done a lot of fighting. The sound was exactly that made by a cat when fighting, and none of the animals made the sound more than once. In one case it was made on the fourth day when the animal's mouth was being cleaned with carbolic; in another (cat XXI—for description see page 221), about two hours after operation as a reaction to air blown into its ear; and in the third (cat III already described) it occurred about three hours after the operation, when the animal was put into the bath. None of the animals repeated the sound (even though cat XXI survived for twenty-two days), however much they were subjected to nocuous stimuli.

Here, again, the vocalization was of a type suggesting that habit formed an important factor, but in this case the sound occurred as an isolated phenomenon, and was not repeated in a reflex and automatic manner as was purring.

Cat III was peculiar in that it gave this growling sound on the first day and no more sounds till the sixth day, when it made a sound somewhere between a growl and a mew while having its temperature taken with a rectal thermometer, at the same time making kicking movements which have been described already. The insertion of a rectal thermometer was an occurrence which was often repeated, and yet only evoked this reaction once, and the same animal on the seventh day gave a series of ten loud and well co-ordinated mews when being turned on its mattress—another response which it could never be persuaded to

repeat. At the end of the seventh day it died—the exact cause being uncertain.

An indefinite cry somewhat similar to a mew has been observed in five animals, of which cats II, III, X and XXI, supply instances. In the other instance the sound occurred once on putting the animal into the bath on the first day; in this animal the section was anterior, from the anterior end of the colliculi to 1·5 mm. in front of the pons, though operated on by the later method. In the case of this sound repetition was occasionally seen, but it could never be reproduced consistently as could purring. This cry is probably similar to the cry made by an animal under an anæsthetic, and which Sherrington [55] [66] has described as occurring also in decerebrate animals while anæsthetized. A normal mew was only observed twice—in cat III, as described above, and in cat XIX, of which details have been already given. In neither case was the mewing repeated, nor could it be produced by subjecting the preparations to nocuous stimuli.

One preparation must now be briefly described to give a clearer picture of the mode of occurrence of pseudaffective responses in general:—

Animal XXI.—Long-haired male; weight 2·5 kilos. (For post-mortem see p. 246). Decerebrated by older method. Had good rigidity one hour after operation, but no good sitting posture adopted. No movements made. Head kept to the left. On putting into bath two hours after operation and blowing into ear when it lay on right side, left pinna retracted, head raised to left and slight low growling sound made. On third day rigidity good, some doubtful pricking of ears to sounds. On fourth day began to kick a lot when turned. On sixth day respiratory rate irregular—about 30 per minute—quickening when the animal was touched. For the first time showed apparent objection to swallowing of stomach tube. On eighth day apparent objection to cleansing of eyes and mouth. Considerable kicking movements when turned, running movements when rectal thermometer inserted. While having eyes cleansed twice made an indefinite cry. Mastication reflexes good—chewed and swallowed piece of meat put into very front of mouth, but on repeating spat second piece out. On twelfth day made movements of resistance against any interference with the position of its head. On thirteenth day respiratory rate raised after turning (apparently as the result of reaction to handling) to 36, to drop to 24 on leaving the preparation undisturbed.

The condition remained as above, but without any more sounds being made till the beginning of the twenty-second day, when the rigidity became less and the reflexes duller, the animal dying at the end of the day.

(*g*) *Spontaneous Movements.*

Spontaneous movements in the form of progression as well as movements of the pseudaffective and defence type have already been described, and it is clear that a distinction must be drawn between the progression movements and pseudaffective responses found after a section through the inferior colliculi to just in front of the pons and those seen when the section was 1 to 3 mm. more anterior, especially on the ventral aspect of the brain-stem. In the former, the pseudaffective responses usually developed only after two to four days, and though they gradually became more active (e.g., cat II), they were never violent. In the latter (as in cat XIX) these movements were seen soon after operation and were much more violent.

Nothing can be added to the description of this second type of animal already given by Woodworth and Sherrington, except to draw attention to the exceptional case with vocalization (cat XIX) already described, and to note that on two occasions such animals have raised themselves from a lying to a standing posture in the incubator and have been found leaning upright against the side of the incubator. Three animals may be briefly described.

Animal XXII.—Female. Decerebrated by older technique. Nystagmus to right and jerky movements of head to right immediately after operation. One hour later found standing in incubator, leaning against side and attempting progression. It died shortly after this. The section was anterior to the superior colliculi and 7 mm. above the pons ventrally with many small punctate hæmorrhages in the mid-brain above the level of the middle of the posterior colliculi. There was a considerable amount of blood-clot lying around the cerebellum and medulla.

With this animal may be compared another (XXIII) in which the section, though low posteriorly, was anterior on the ventral aspect, and one (XXIV) anterior both on the dorsal and ventral aspects.

Animal XXIII.—Adult male. Post-mortem, see p. 248, and figs. 22 and 23. Decerebrated by older technique. Rigidity good. On second day on cleansing the mouth with carbolic it kicked violently and moved about a great deal. The respiratory rate remained about 19 to 28 during "life"; it was constantly making progression movements spontaneously, but only kicked violently when touched. Died on sixth day.

Animal XXIV.—Female. Decerebrated by older technique. Three-quarters of an hour after operation found standing in incubator leaning against the side with its head down biting the wire netting floor. It was making violent kicking movements. It was taken out of incubator and then remained quiet,

but showed auditory reflexes. After another forty-five minutes it was put into the bath, when it again had a paroxysm of most violent movements. It died about four hours after operation. The section passed through the superior colliculi and was 4 to 6 mm. in front of the pons ventrally. There were three small punctate hæmorrhages in the mid-brain just below the posterior colliculi, and considerable subtentorial hæmorrhage extending around the cerebellum and medulla and some way down the cord.

The movements in these anterior sections recur in paroxysms every fifteen to forty-five minutes, the intervals being shortened if the animals are exposed to stimuli such as touches, shakes or sounds. On the other hand, immediately after such a paroxysm there is a refractory quiescent interval, and in such an interval an animal of this type will lie quietly passive in a condition of simple decerebrate rigidity while a wound is stitched, although fifteen minutes later it may react with the utmost violence to a slight stimulus such as a jar or sound. Here, again, there is no evidence at all of any conscious sensation or emotion.

In these animals the movements usually resulted in reactionary hæmorrhage and it has never been found possible to preserve them for more than a few hours. A contributory factor to their death may well have been the respiratory irregularities described by Macleod [34], though in our animals movements were so active and general that it was not possible to judge whether there was any hyperpnœa other than that secondary to the exercise.

Slight vomiting just before death was in these a common occurrence.

Of other movements that have been observed two are worthy of notice. One has been described in cat II—an apparent attempt to reach a sore spot on its skin with its fore-paws, and the other was a complex scratch movement made by cat XIII, which four hours after operation curled itself up into a flexed position, although it had good extensor rigidity, and made (almost completely) the movement used by a cat when scratching the back of its neck with one of its hind limbs.

It is noticeable that violent movements and vocalization were only seen in one animal out of twenty-seven operated on by the later technique. In the latter technique the section had a different obliquity, passing usually from just in front of the corpora quadrigemina to just *below* the anterior border of the pons, and in the one exception where violent pseudaffective movements were made soon after operation and where an indefinite cry was also made, the section had passed just in front of

the superior colliculi to 1·5 *millimetres in front of the pons.* The centres responsible for this reaction therefore probably lie nearer the ventral than the dorsal side of the brain-stem, since it is the level of the section on the ventral aspect that makes the most difference (contrast however cat XXIII). And yet the animals operated on by the later method showed the other more common pseudaffective responses and were very liable to make progression movements, in spite of the different obliquity of the section.

(*h*) *Acoustic Reflexes.*

Acoustic reflexes have been described in the case of animal II and a similar lifting of the head to the left was also seen in cat III, commencing about two hours after operation, and some such reflex was also present in VI, IX, XIV, XVIII, XIX, XXI and XXIV of the animals so far described and also in animal XXVI to be described later. No doubt the other acoustic reflexes described by Forbes and Sherrington [14], such as wagging of the tail in response to high notes, may have occurred in many of the animals, but their position in the bath was not favourable to its observation and it was only noticed in a few animals. Movement of the head and of the fore-limbs was observed in many animals and was usually particularly noticeable, as in animal II, in those cases where the rigidity of the neck muscles was uneven so that the head tended to go to one side or the other. Apparently the stimulus increased the rigidity, and this being uneven, movement of the head resulted. In no case did an animal raise its head to sounds regardless of the position it was lying in; invariably the head was only moved to one side or the other.

The auditory reflexes became usually much more brisk after two or three days, and might often be seen at this stage when there had been no sign of them earlier, so that their absence could not be presumed unless the preparation had survived at least three or four days.

The greater reaction to high notes, resembling the roof-cries of cats, noticed by Forbes and Sherrington, was often confirmed; on the other hand, in many animals the most effective sound was a small scratching noise, and an animal would often react promptly by raising its head if a piece of paper was crumpled up at a distance of one or two yards. These sounds are similar to those made by a mouse. One reaction to sounds sometimes observed was the extrusion of the claws in the fore-limbs, which may perhaps be a guide to the nature of the reflex. Animals would react to these slight noises even though there was a

constant loud noise from the motor and stirrers, to which no reaction was shown except when it was started after an interval of rest. It is worth noting that in the older technique a reaction to sounds was noted in most animals where the section passed in front of the inferior colliculi to about 2 mm. in front of the pons, but even so not in all, and that it was seen in one in which the section commenced in the middle of the inferior colliculi and passed to the same level. It was never seen in sections by the later method with a different plane of section, if this passed from the anterior end of the superior colliculi to the anterior end of the pons, but was seen in one case where the section passed from just in front of the superior colliculi to 1·5 mm. in front of the pons, in the animal which has been referred to as having spontaneous violent movements and vocalization. It would appear therefore that here too the level of the section ventrally makes more difference than the level of the section dorsally, and that the highest link in the chain for this reflex may be nearer the ventral than the dorsal part of the brain-stem.

On the other hand, in cat XXIII (see figs. 22 and 23 and p. 248), no auditory reflex was observed, though the section was anterior on the ventral aspect.

(*i*) *Nystagmus.*

Spontaneous nystagmus was seen in several preparations, but usually in the first few hours only after operation, and probably as the result of irritative effects of hæmorrhage.

In animal XXII already described there was a jerky movement of the head to the right accompanied by nystagmus, which was kept up spontaneously during the few hours of life.

Two animals may be briefly described.

Animal XXV.—Adult male. Decerebrated by earlier method. Two and a-half hours after operation had extreme rigidity and made running movements when touched. Five hours after operation had paroxysms of violent fighting movements, claws extended, springing movements also made. General appearance of anger, but all movements inco-ordinate. Several paroxysms at about fifteen-minute intervals. Pinna reflexes brisk. No definite auditory reflexes. Just before the attacks there was some increase in the already very great rigidity, with some retraction of the head, which was also bent to the left. With this there was nystagmus to the left and jerky movements of the head to the left, present to a slight extent all the time, but exaggerated with the commencement of a paroxysm. Animal died in the night, vomiting slightly before death. The section passed in front of right superior colliculus and through the middle of the left superior colliculus dorsally to emerge

3 mm. in front of the pons on the right and 1 mm. in front of it on the left. There was no sign of hæmorrhage into the stump of the brain-stem but a clot about the size of three peas was lying over the stump above the tentorium. No detailed examination was made.

Animal XXVI.—Female. Post-mortem, see p. 249. Decerebrated by earlier technique. Good rigidity, head to left, good reflexes, lifts head to left to noises on first day. No nystagmus.

On second day head lifted to left in reaction to sounds and this accompanied by nystagmus to left.

On third day respiration very fast. Reflexes very sluggish and almost absent. Some convulsive movements of the legs, but no eye movements. Died during the night.

The nystagmus when seen was of a usual type with rapid and slow components, but the animal described above and animal IX which developed nystagmus on the ninth day when meningitis occurred were the only ones where it has been observed, except in the first few hours after operation.

(*j*) *Glycosuria.*

It has been suggested by J. Mellanby [41] that there is a centre in the brain above the medulla which controls sugar metabolism, this theory having been built up on the prolonged glycosuria which follows decerebration as compared with that seen after decapitation. But Mellanby's decerebrate preparations were made by Langley's [29] starch injection method, so that nothing definite was known of the real level of the lesion, nor of the changes resulting in the pituitary. At the same time the glycosuria observed was only investigated over a matter of a few hours after operation. We can, however, amply confirm the long duration of glycosuria found by Mellanby after decerebration; thus in one animal urine obtained by catheterization from the bladder twenty-four hours after decerebration still contained quantities of sugar.

On the other hand, the glycosuria does not continue indefinitely. Thus the urine of cat VIII contained no sugar on the third day; in another animal (XV) urine voided forty-seven hours after operation contained no sugar. This animal had previously voided fæces and urine about thirty hours after operation; so it appeared to have ceased to secrete sugar, at any rate after thirty hours. In no case has any glycosuria been observed after the second day—though observations on this question have only been possible in preparations kept in the incubator. Nor does it appear possible that the glycosuria ceases as

the result of loss of glycogen. In cat V urine collected on the sixth day showed no sign of sugar, and yet when the animal was killed shortly afterwards the liver gave a normal glycogen reaction with iodine. In cat XXI, urine taken from the bladder after death contained no sugar, but the liver was not normal.

The theory put forward by Mellanby does not, therefore, explain the facts—though the more prolonged glycosuria compared with that of the decapitate preparation certainly requires some explanation. Further, experiments on this point are planned for the near future. The glycosuria we have observed occurs even when the body temperature has been subnormal for quite a short while, and we do not think that it is to be explained as merely secondary to a fall in body temperature as is suggested by the experiments of Morita [44] on rabbits; nor do we find, as he did, that it ends usually only on exhaustion of the liver glycogen.

Chapter IV.—Unilateral Decerebration.

A series of semi-decerebrations as chronic experiments was undertaken on the suggestion of Professor Sherrington, in order to study the resultant decerebrate rigidity. Seventeen cats were operated upon of which four died at once from hæmorrhage or accidents of anæsthesia. The remaining thirteen experiments are not sufficient to answer many of the questions that prompted the undertaking, and further work has been planned along the same line. It seems worth while, however, to include here a brief description of the semi-decerebrate preparations for the sake of comparison with the results of complete decerebration.

Operative Technique.

Cats were used under chloroform or chloroform and ether anæsthesia by the open method. A small mid-line incision was made in the neck and the right carotid tied. The left carotid and vertebrals were controlled at the proper time as in the bilateral operation. The skin and muscle were reflected from the right side of the head. The underlying skull was quickly removed so as to expose the right cerebral hemisphere. The dura was reflected. Then, with the arterial supply shut off, the operator passed a flat bone spatula (a properly shaped salt-spoon) over the top of the right cerebral hemisphere, until it touched the falx, and swept it downwards to the tentorium and outwards, carrying

away all of the hemisphere except the frontal pole, which could be quickly scraped out. A part of the inferior colliculus was usually thus left intact. This was reflected forward from the surface of the cerebellum and removed by a bent bistoury, together with any of the mid-brain that may have remained ventrally above the top of the pons. The cavity was quickly filled with cotton wool in hot saline and the vertebral arteries released. Bits of fresh muscle were usually necessary to arrest all bleeding before the left carotid artery was released. The cavity was filled with physiological saline before closure.

In six of the experiments the cavity was filled with a melted paraffin-vaseline mixture after removal of the hemisphere. One of these animals lived only eleven hours, and four died on the day following operation. Three of the animals became dull and vomited just before death. Compression beneath the wax was suspected, and when the sixth animal became dull two days after operation the wound was opened and the paraffin removed. There was a gush of fluid from beneath showing increased pressure. The animal improved temporarily, but died on the day following from broncho-pneumonia. Examination of the brains where the dead space was filled with saline, as described above, showed a varying amount of swelling of the remaining hemisphere across the mid-line. The animals whose cranial cavities were filled with normal saline rather than wax lived to between two and forty-two days after operation. The conclusion is evident: that swelling of the remaining brain tissue against the wax was sufficient to cause fatal compression of the lower centres.

It was found advisable to suspend the more active animals in a hammock provided with slits for the legs to come through.

The removal, which was always on the right side, extended in each case down to the mid-brain. Two types of removal were made: (1) anterior, where the decerebration passed above the inferior colliculus, leaving a varying amount of superior colliculus intact and most of the mid-brain ventrally (in this type the red nucleus was not molested); (2) a posterior removal where the section passed from behind the inferior colliculus dorsally, to the anterior margin of the pons ventrally. In this type one red nucleus was removed. Post-mortem examination showed that the removal followed the median sagittal plane with surprising accuracy, except for the fact that in two cases the spatula passed about 2 mm. to the right of this plane, leaving that thickness of mid-brain and thalamus, and in several cases a very small amount of the left thalamus or mid-brain was removed.

Forced Movements and Attitude of Head.

The animal's head was *usually* held to the left at the close of the operation, and in *every case* eventually. This attitude depended on rotation of the occiput downward and to the left, so that the chin was up on the opposite side and the neck bent to the left. The displacement therefore consisted of retraction of the neck and clockwise rotation of the head on the shoulders, the head being carried to the left away from the side of removal. Those that were able to walk fell to the left or walked around in a circle to the left. If the animal was laid on its right side it raised its head up to the left and, pushing with the right fore limb, rolled about the cage. When lying on the left side the preparation frequently lay quietly but pressed the occiput against the floor. These attitudes were eventually assumed in every case (except that in two animals no note was made of any forced circus movements). In all of the anterior sections, as described above, and in the one posterior section where about 2 mm. thickness of the mesial portion of the mid-brain and thalamus were left intact, the animals turned their heads first to the right on recovering from the anæsthetic. Within one to five hours in each case this movement was reversed and the typical movement of the head to the left appeared, associated with forced movements to that side. The short duration of this preliminary turning to the right in the anterior section cases before reversal suggests that some structure is spared by the anterior or lateral removal, which is stimulated by traumatic irritation, but later becomes paralysed or unable to cope with a contrary tonic influence.

After the effects of stimulation had passed off, the head was held constantly in a position similar to what has been termed the cerebellar attitude. In lesions of one side of the cerebellum, the occiput is said to turn in that direction and the head to be retracted to the side of the lesion. In semi-sections of the mid-brain, at either a high or a low level, the movement is *away* from the lesion. This was a constant finding in these experiments. It may be explained perhaps by the fact that one side of the cerebellum is in close anatomical relation with the other side of the mid-brain. Muskens [45] has made extended observations on the effect of lesions confined to the posterior longitudinal bundle. Circus and rolling movements followed such injuries. It is difficult to make explicit applications of his results to the movements described here however.

The Side of Permanent Extensor Rigidity.

Sherrington noted in 1898 [54], working with acute experiments, that unilateral decerebration through the mid-brain was followed less regularly by decerebrate rigidity than complete sections of the brain-stem. It appeared most often on the same side as the decerebration and was occasionally observed to subside and reappear. He noted in a monkey and in cats that after right semi-decerebration, the right limbs were held in tonic extension, the tail incurvated to the right with the concavity to the right. The head was turned to the right and retracted. The left fore limb and knee were distinctly more flexed than would be expected in paralysed limbs. Thiele [57], in acute experiments, likewise noted ipsilateral rigidity after semi-section of the mid-brain, and that if the section were more anterior, through the superior colliculi, the rigidity tended to become *contra*-lateral, only a little remaining on the ipsilateral side.

The chronic experiments described below show that some of the above post-operative reactions are reversed after an initial stage of stimulation.

In the following experiment, No. P1, after removal of the right hemisphere down to the mid-brain, the preparation was suspended in a hammock in erect position with legs passing through hammock holes. The animal's head was at once turned to the right and there was extensor rigidity in all four limbs. There was slow nystagmus with the quick component to the right. At intervals there were spasms of running movements during which periods the nystagmus became more rapid. The rigidity of the left limbs became progressively less marked until two and a half hours after the close of the operation, when the right fore and hind limbs were found to be still in tonic extension sufficient to support the weight of the body. Both left limbs, however, tended to assume a flexed posture and were held thus a little rigidly. The spontaneous nystagmus had disappeared. At intervals spasms came on resembling those mentioned above, except that now the right limbs ran and the left limbs became still more flexed, especially the fore limb. At these times the eyes opened, the head turned to the right, and there reappeared a very small amount of nystagmus to the right. Left pupil widely dilated, right pupil less so. Rectal temperature 37° C.

Four and a half hours after operation—head was now turned constantly to left.

Twenty-four hours after operation—head to left and body, including tail, curved with the concavity to the left. Extensor rigidity marked on right side. Left limbs held in tonic flexion so as to resist passive extension. Occasional clawing spasms, at which times the head was retracted. The preparation was

taken from the hammock and it swallowed some milk which was poured into its mouth.

Three days after operation there had occurred a surprising change. The extensor rigidity was now in the left limbs. When suspended in the hammock and quiet, the right limbs maintained a flexed position. It was not possible to say whether there was any flexor tonus however, as the right limbs were now voluntarily snatched away when touched and were used to scratch the observer's hand whenever he attempted to administer food. The left limbs were never used in this way. When placed on the floor the animal walked slowly in a circle to the left, reeling and falling to the left. The head was still held to the left and the jaw tightly clenched. The pupils were now equal. Temperature 38° C. Late the same night condition unchanged.

Four days after operation. The front end of hammock had fallen, so that the animal's head hung almost straight down. Animal dead.

Post-mortem: A subdural hæmorrhage was found extending over the left hemisphere, under the base of the brain and down the cord to the upper dorsal region. Some of the hæmorrhage appeared to be more recent than other parts. The operative removal extended back to the middle of the inferior colliculus but had not quite come to the mid-line, so that 2 mm. of the mesial part of the mid-brain and 3 to 4 mm. thickness of the posterior part of the right thalamus were spared. A very thin slice of the mesial part of the frontal lobe was likewise spared. Interrupted serial sections were cut of the whole left hemisphere, mid-brain, pons, and medulla. There was no area of destruction or softening.

It seems probable that the behaviour of the cat immediately following the operation was due to stimulation which gradually subsided during the succeeding two days. During that time various reactions disappeared or were replaced by opposite reactions. The early rhythmic intensification of these reactions also suggests a response to irritation, i.e., clawing or running spasms associated with nystagmus to the right, head turning to the right and increase in the left-sided flexor rigidity. The spontaneous nystagmus disappeared a few hours after operation. The head, which had been first thrust to the right, came later to the mid-position and shortly afterwards was turned to the opposite side, to remain constantly in this typical position with corresponding curving of the body to the left. The occasional spasms of running movements continued for two days. At the end of that time the flexor rigidity of the left limbs disappeared and was replaced by extensor rigidity; while the extensor rigidity disappeared on the right side to be replaced by the position of flexion in the right limbs when at rest.

The unusually long duration of the signs of stimulation may possibly be explained by the evidence of older hæmorrhage at autopsy, which

had not been enough to cause compression until the accident which led to the animal's death.

Shortly after operation this animal resembled those described by Sherrington in acute experiments. Extensor rigidity was present on the same side as the decerebration, but *after* the irritation stage had passed off it was on the contralateral side. The same was true of all other animals where the section passed through the anterior part of the mid-brain. Extensor rigidity appeared on the contralateral side either at once or after a preliminary stage of flexor rigidity.

Variations after Posterior Semidecerebration.

On the other hand, when the level of removal was through the lower mesencephalon or junction of the mesencephalon and pons, the results were less constant and subject to less symmetrical variations. For example, take the following experiments :—

P2. The removal was of the posterior type. Bilateral-extensor rigidity developed on the first day. On the second day a varying degree of flexor rigidity of the left fore-limb appeared, with extensor rigidity of the other three limbs.

Experiment P3 showed, one hour after operation, extensor rigidity of the left fore-limb, the other limbs being flaccid. At the end of five hours the left fore-limb showed flexor rigidity, the other three extensor rigidity.

Experiment P4. Bilateral-extensor rigidity with considerable retraction of head associated with the usual turning to the left.

Experiment P5. A more detailed account of this animal is given on page 234, but it may be noted here that on the day of the operation there was bilateral rigidity. This was followed by some variation and then for several days, when not moving about, the fore-limbs were held in rigid flexion, the head held to the left and the neck flexed sharply on the fore-paws, while both hind-limbs went into tonic extension. This was followed by weeks of activity associated with a variable amount of extensor tone in the left fore and hind limbs.

This variation in the tone of the flexor and extensor systems in posterior removals suggests that some structure responsible for preserving a symmetrical tone pattern has been injured.

Flexor Rigidity.

After more anterior semi-decerebrations, the post-operative pattern was tonic-extension in the limbs on one side and tonic-flexion in those of the other. In certain cases, e.g., P1, the extensor rigidity appeared

first on the ipsilateral side with flexor rigidity on the other side. This was, however, shortly reversed.

It may be suggested in unilateral removal, after all stimulation effect has passed off, that control has been removed from some structure whose unantagonized action produces tonic-extensor rigidity in the contralateral limbs and tonic-*flexor* rigidity on the ipsilateral side. When the decerebration is bilateral the flexor element usually disappears and is superseded by extensor rigidity on both sides. . But, as is shown elsewhere in this paper (Exps. III and IV, p. 199), even in the complete decerebration experiments, tonic-flexion occasionally replaces tonic extension.

Thiele [57] and Graham Brown [9] found that electrical stimulation of one side of the mesencephalon in the region of the red nucleus produced ipsilateral flexion and contralateral extension. The latter observed that there was an after-discharge following cessation of stimulation. It is difficult to be certain exactly what tract is stimulated by these workers. Bilateral stimulation produces bilateral extension. Their work indicates that there are structures in the mid-brain, possibly the red nuclei, which take part in the control of posture. (Also Magnus [40].) It is not necessary, nor possible, to identify this postural mechanism with that responsible for flexor or extensor rigidity.

One of the conclusions that may be drawn from these chronic preparations is that there is a mechanism by means of which there may be induced increase of tone in flexor muscles at the expense of tone in the muscles of the extensor surfaces. This flexor rigidity tends to alternate with extensor rigidity, appearing frequently in the limbs of the side opposite to that in which extensor rigidity occurs.

Wilson [63] describes decerebrate attitudes in clinical cases associated with mesencephalic lesions. In his fig. 13, p. 247, the child has assumed a position resembling the attitude of unilateral decerebrate rigidity, with arm and leg of one side extended, as the author points out. It is interesting to note, however, that in addition the limbs of the opposite side are held in a sharply flexed attitude.

Eye Changes.

In every case where the corneal reflex was examined it was present on both sides. There was some variation, but the right pupil was dilated in the great majority of cases. This was most noticeable on the

first day after operation. Nystagmus was observed only in one experiment. This was in P1, see p. 230, and passed off with other evidences of stimulation. The quick phase was toward the side to which the head was turned.

Temperature Control.

Most of the animals preserved some power of temperature control if not exposed to extremes. In three experiments there was no evidence of control whatever, the temperature falling to between 34°5 C. and 24°5 C. Those animals which survived longest maintained a normal temperature. In experiment P5 it was noted in a cold room that the animal shivered equally in the limbs of the two sides. In this animal the removal extended down to the anterior end of the pons and was carried well over to the mid-line. Removing the other half of the brain at the same level would have put an end to shivering (see p. 205).

Experiment P5 was described in part above, but as the animal lived forty-five days before being sacrificed, a brief account of the post-operative behaviour may be added.

The right side of the brain was removed up to the mid-line and down to a level below the inferior colliculus. The cavity was filled with saline. After the operation the right pupil was found to be dilated, the left contracted, both corneal reflexes present. For two days there was bilateral extensor rigidity which became variable. The animal was examined by Dr. Henry Head and Dr. Riddoch, who called attention to the fact that when it lay on the left side the left fore-limb was held in tonic flexion with claws extruded, and that ten minutes after turning over on to the right side the right fore-limb assumed the flexed attitude. This was not a constant finding at later examinations. The head was consistently turned to the left and the body and tail curved with concavity to the left. Milk was swallowed when placed on the back of the tongue with a tube. The animal clawed with right paws only. On the third day the fore-limbs were flexed sharply and paws crossed with the head bent down upon them and with occiput a little to the left. Both hind limbs were extended strongly most of the time. When disturbed there resulted spitting and clawing or purring appropriately. This continued for four or five days with gradually increasing activity. During the first week the temperature fluctuated between 40° C. and 37°8 C. After this the temperature settled down to normal, about 38°6 C.

Between one month and six weeks after operation the following notes were made. The cat had gained in weight. The head was rotated still, with occiput to the left and chin to the right, the neck, body and tail being curved with the

FIG. 6.—Experiment P5. Six weeks after complete removal of right side of brain, including mesencephalon. Tail curved to left, left legs extended, toes of left hind paws fanned, both fore paws rotated with pads a little towards the right. All of these attitudes are characteristic, as well as the rotation of the head on the shoulders.

FIG. 7.—Same animal as fig. 6.

concavity to the left (see figs. 6 and 7). When not lying quietly, the animal walked around in a circle to the left. She purred frequently and growled or spat occasionally. Even when restless from hunger, she never discovered meat or milk placed before her unless her nose was pushed down into it, resembling Goltz's dog in this respect. After she realized what it was, she ate or drank almost normally until satisfied.

Cranial nerves: She gave no evidence of smelling food from any distance but may have done so at close range. She was blind, bumping into objects frequently or walking off the edge of a board unawares. Her eye grounds were examined by Mr. Leslie Paton, who made the following note: Right optic disc chocolate colour with a sharply defined ring of very glistening green around it. Vessels normal in calibre. Upper part of fundus shows a little speckling of green passing down to a deeper green in the lower part. Left optic disc much the same as the right. The eye movements were examined by Dr. Gordon Holmes. The external ocular movements were normal and the range to either side seemed to be full. The right pupil did not react either directly or consensually to light, while the left pupil contracted to light in either eye. The right pupil did contract with some movements of the eyes, however. Also, tickling the nose or blowing into the eye caused very definite contraction of the right pupil. Reaction to pin prick and corneal reflex indicated intact fifth nerve on both sides. Hearing was acute and sounds were well localized. All other cranial nerves appeared normal.

Extremities: There was considerable variation but on the whole there tended to be tonic extension of the limbs of the left side (the opposite side to the removal). When suspended, the left limbs were extended and the hind toes fanned (see fig. 6). The left fore-paw was inverted and the right fore-paw everted. The knee jerks varied but the left was usually the more brisk.

Sensation: Pinprick was resented equally on the two sides. Touching the hair on the right side produced a reaction. The same stimulus on the left flank was ignored.

Heat control: Shivered symmetrically when in a cold room.

Gait: The right fore-foot took a longer step than the left and the foot was raised higher. She turned in a large circle to the left. Occasionally she stepped on the dorsum instead of the plantar aspect of the left fore or hind paw, and the left hind-paw at times interfered with the fore-paw. When excited, she walked about in a very small circle. It was noted by Dr. S. A. K. Wilson that the left fore-foot was advanced at each step with a tremor of the paw. At times she stumbled to the left.

Affective reactions: She purred when stroked or after feeding, growled when eating meat, and occasionally spat and scratched. When another cat was brought near her, no notice was taken until the visitor mewed. Then P5 growled and became suddenly rigid as though listening. After a little time she started toward the visitor who was moving softly, and continued until her nose bumped into the visitor. Then P5 leaped back and stood with all hair raised on back and tail. The visitor moved away and at that moment P5 struck out

as though to attack her, spitting. The visiting cat was removed and P5 walked around very rapidly in a small circle.

Six weeks after the operation, the animal in excellent physical condition was sacrificed under ether-anæsthesia. Post-mortem examination showed the right side of the brain to have been thoroughly removed up to the mid-line. Several shreds of what may have been cortical tissue were left. These were not connected with the brain-stem. The right thalamus and mid-brain were removed down to a plane which passed through the anterior margin of the pons ventrally, and just behind the inferior colliculus dorsally. A complete microscopical report could be made as an unfortunate accident destroyed most of the material while it was being prepared.

Chapter V.—Microscopical Anatomy of Specimens.

(*a*) *Development of the Mid-Brain.*

In lower vertebrates (e.g., fishes) the mid-brain is a centre of great importance, controlling the individual response to environment. With the development of the optic thalamus and the geniculate bodies (reptiles) the importance of the mid-brain for co-ordinating visual stimuli is decreased, and in man with the elaboration of the visual cortex the anterior corpora quadrigemina of the mid-brain become rudiments. There is likewise a forward displacement of the sensory centres to the ventral part of the thalamus, which continues to develop along with the sensory cortex. The auditory paths move out from the mid-brain to the internal geniculate body and auditory cortex. The mid-brain has therefore a progressively decreasing functional importance proportionally during phylogenetic development.

Microscopically the red nucleus of a lower vertebrate is composed of large cells of motor type from which arise the rubrospinal tracts. Higher in the phylogenetic scale there appear smaller cells in the red nucleus and, as von Monakow [43] has pointed out, it is possible to distinguish an orally placed group of smaller cells, the nucleus parvicellularis of Hatschek [19] or chief nucleus, from the more caudal giant cells, or nucleus magnocellularis. The small-celled nucleus develops *pari passu* with the thalamus and cerebral cortex and is connected with them. In anthropoids and man this nucleus of small cells makes up the major part of the red nucleus, while the giant-celled part has become very small and, as a result, the rubrospinal tract has greatly diminished in volume. Nevertheless, because of the great increase in size of the small cell part, the red nucleus of man is almost twice as

large as that of the cat in proportion to the vertical diameter of the mid-brain of each species [43].

(*b*) *Anatomy of the Mid-Brain.*

The anatomy of the mid-brain of a cat may be quickly reviewed by reference to fig. 8, which is a drawing from a lateral longitudinal section through a cat's brain. It will be seen that a section through the mid-brain may leave or remove according to its level a number of

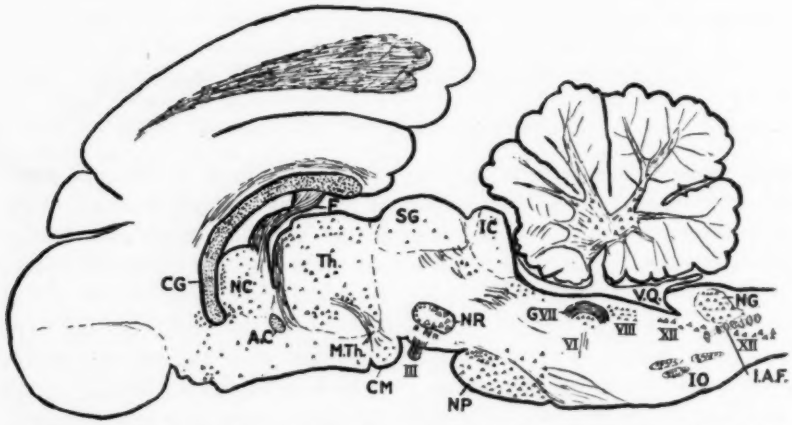

FIG. 8.--Sagittal section of cat's brain a few millimetres from the median plane, drawn from two adjacent sections, one stained by Loyez's hæmatoxylin method and the other by Nissl's method. This as well as all the other microscopical drawings was made with the help of an Edinger Drawing Apparatus kindly loaned by Dr. Gordon Holmes. Diagrams in succeeding figures are taken from this drawing reduced to natural size. C.C., corpus callosum; N.C., nucleus caudatus; A.C., anterior commissure; F., fornix; Th., thalamus; M.Th., mamillo-thalamic tract or bundle of Vicq d'Azyr; S.C., superior colliculus; I.C., inferior colliculus; N.R., nucleus ruber; N.P., nuclei pontis; III, root of III nerve; G VII, genu of VII nerve; VI, nucleus and root of VI nerve; VIII, dorsal nucleus of VIII nerve; XII, nucleus of XII nerve; V.Q., fourth ventricle; I.A.F., internal arcuate fibres splitting XII nucleus.

structures, the anterior and posterior corpora quadrigemina, the third and fourth cranial nerve nuclei, the whole of the tegmentum, the red nucleus, &c. The red nucleus is circumscribed by a felt-work of fibres. The caudal two-thirds of the nucleus is made up of giant cells as indicated. The oral one-third only is made up of small cells.

According to Hatschek, this phylogenetically younger nucleus parvicellularis is in relation with the nucleus dentatus of the cerebellum, while the older nucleus magnocellularis is interposed between the

cerebellar nucleus globosus and emboliformis above and the descending rubrospinal tract. He concludes that this close anatomical relationship of the nucleus magnocellularis with the cerebellum and Monakow's bundle constitutes the primitive path of nerve impulses for automatic movements. Other tracts converge on the red nucleus. Von Monakow describes a fronto-rubro-tegmental pathway. The fibres thus indicated arise in the frontal cortex and pass down via the red nucleus to the tegmentum of the mid-brain and formatio reticularis of the pons, from where they are supposed to send a relay to the spinal cord. Wilson [62] has shown that there is a considerable tract of fibres from the globus pallidus which passes across Forel's field to the anterior capsule of the red nucleus. The principal red nucleus efferents are the rubrospinal tracts of Monakow which cross the mid-line in the fountain decussation of Forel. This tract arises wholly in the giant cells, according to Cajal [10]. Von Monakow describes some fibres as coming from the cells of medium size. Certainly the tract arises chiefly from the nucleus magnocellularis, and comparative anatomical studies show that this part of the red nucleus varies directly in size with that of the tract in most animals, and both are small in man. Efferent fibres of importance also pass from the red nucleus to the tegmentum and formatio reticularis, as well as to the thalamus and frontal cortex.

Because of its venerable phylogenetic history and its wide anatomical connections, the red nucleus has been rather heavily burdened with theoretical functions. It is therefore of importance to note carefully the state of preservation of this nucleus in the experimental animals.

(c) *Results of Anatomical Examination.*[1]

Animal I.—Death on the eighteenth day after decerebration. Post-mortem performed about thirty minutes after death, immediately after removal from bath. Along the scalp incision there was an area of superficial cellulitis. No evidence of intracranial tension. A lump of wax filled the cranial cavity conforming to its outline. On removing the wax a thin layer of pus was found beneath it. The brain-stem and spinal cord were removed and placed in formol. See photographs of brain-stem, figs. 9 and 10. Incision A—B, fig. 9, corresponds to line A—C, fig. 11.

[1] In a number of experiments the preparations died and remained in the warm bath long enough for the brain-stem to become soft. In such cases no microscopic examination was possible.

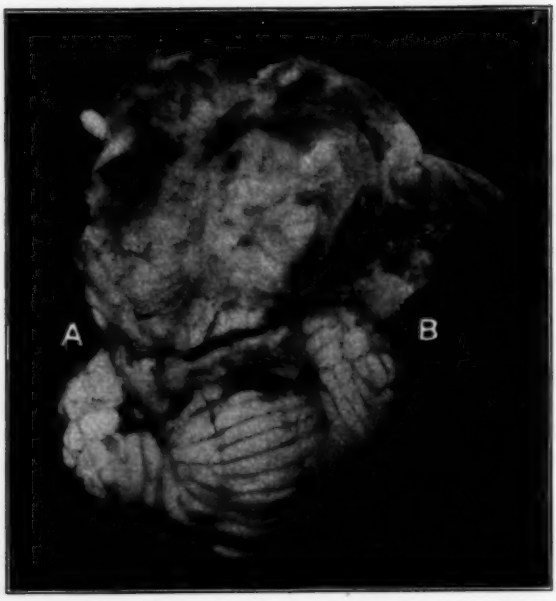

FIG. 9.—Experiment I. Photograph of brain-stem taken from above the cerebellum.

FIG. 10.—Experiment I. Lateral view of brain-stem showing the temporal pole which was not removed.

The only remaining portion of the cerebral cortex was a small part of the right temporal lobe which was attached to the brain-stem by a thin piece of nervous tissue overlying the infundibulum. Thus the pituitary and probably its blood-supply were preserved. All of the basal ganglia were removed above line A—B, fig. 11. A little below the

FIG. 11.—Experiment I. All of the tissue above line A—B was removed. A second incision at line A—C was almost complete as indicated. Dotted area represents extent of softening on right side.

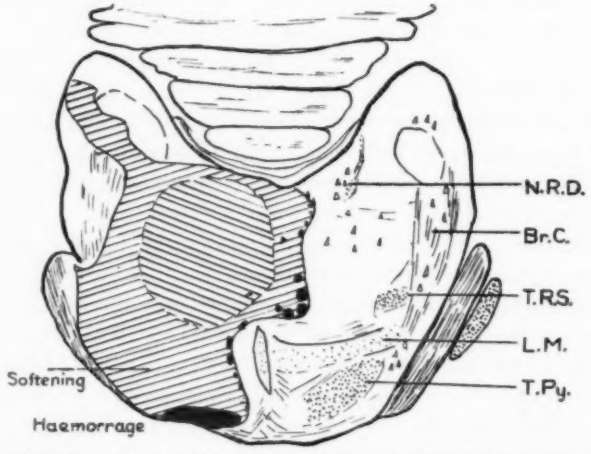

FIG. 12.—Experiment I. Drawing made with the aid of an Edinger apparatus, from a section stained by Loyez's hæmatoxylin method for the fibre tracts. The cell groups indicated by small triangles were added from the next section in the series stained by Nissl's method. The large area of softening has an outer part filled with compound granular corpuscles and an inner area which contained no cellular elements. N.R.D., nucleus of descending or mesencephalic root of V nerve; Br.C., brachium conjunctivum; T.R.S., rubro-spinal tract; L.M., medial lemniscus; T.Py., pyramidal tract.

level of the tentorium was an incision A—C, almost entirely severing the brain-stem. It began dorsally just behind the inferior colliculus and passed ventrally on a plane just caudal to the anterior end of the pons, but did not quite completely sever the cerebral peduncles. This incision had severed the right fifth nerve close to the pons.

After fixation, block I, including the tissue above and below incision A—C, and block II, just below this, were cut in series and alternate sections were mounted and stained by Nissl's method and by Loyez's hæmatoxylin method. The latter method demonstrates the tracts clearly. The rest of the central nervous system was stained by the Marchi method for degenerated fibres, and cut and mounted in series.

Microscopical examination shows that the red nuclei are present in the segment of nervous tissue above the incision A—C. All of the giant cells in both nuclei show marked chromatolysis, although the medium and small sized cells were for the most part normal. This indicates that the descending fibres of Monakow's bundle had been severed. Immediately below the incision A—C was an area of softening occupying practically the whole of the right half of the upper pons, as shown by the heavily dotted area in fig. 11, and passing across the mid-line dorsally. This area (see fig. 12) was separated by a line of hæmorrhage from the normal tissue of the left side. Even had the descending red nucleus fibres of this side not been severed by the incision A—C, they would have been destroyed in this area of softening. There was no evidence of encephalitis anywhere within the nervous tissue. The softening was evidently the result of hæmorrhage at the time of operation. If the experiment had been acute instead of chronic, it is quite possible that this area would have been passed as normal, although it was doubtless functionally inactive from the start.

The cerebellum was normal and it should be noted that although there was, of course, interruption of the tract connecting cerebellum with red nucleus and thalamus, the ventral spino-cerebellar tract of Gowers was intact and showed no degeneration. There were degenerated fibres in the middle cerebellar peduncles, as would be expected from the injury to the nuclei pontis, and there were a few degeneration granules in the restiform body. Vestibular nuclei were intact.

The Marchi sections beginning in the pons and passing downwards showed degeneration as follows. (Refer to drawings, figs. 13, 14, 15, 16, 17, 18; black dots indicate degenerated tracts.)

(1) The pyramidal tracts show rather fine degeneration-granules. It was noted that immediately below the pons degenerated fibres came off from the pyramidal tracts, decussated at once and passed outward among the fibres of the trapezoid body (fig. 14). They could not be definitely traced beyond the superior olivary nucleus and the medial trapezoid nucleus. Below the corpus trapezoidium also, the decussation of these pyramidal fibres continued. Their ultimate destination

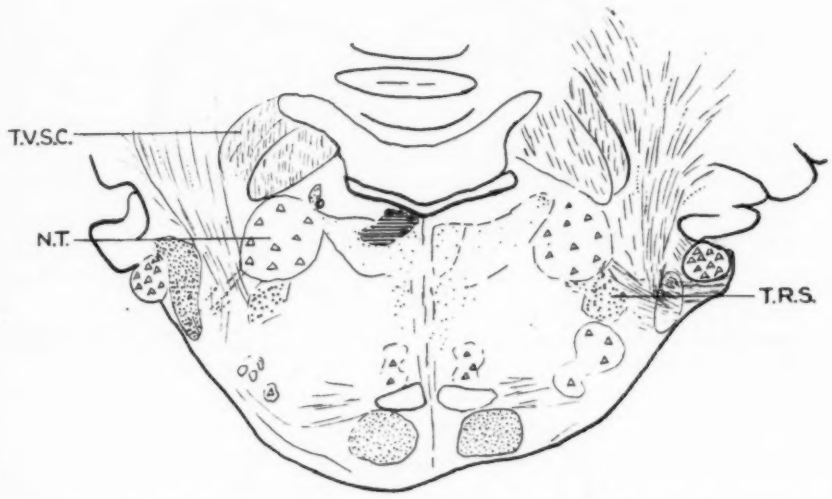

FIG. 13.—Experiment I. Section prepared by Marchi's method to show degenerated fibres. The area of softening described above (fig. 12) is represented at this level only by a small area beneath the fourth ventricle. T.R.S., rubro-spinal tract; N.T., nucleus of trigeminal nerve; T.V.S.C., ventral spino-cerebellar tract.

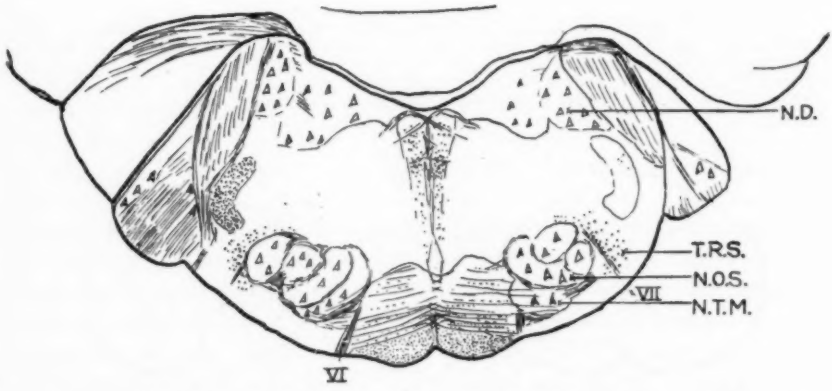

FIG. 14.—Experiment I. Marchi stain. Degenerated fibres may be seen to decussate in the mid-line and pass outward in the trapezoid body as far as the medial nucleus. N.D., Deiters' nucleus; T.R.S., rubro-spinal tract; N.O.S., nucleus of the superior olive; N.T.M., medial nucleus of the trapezoid body.

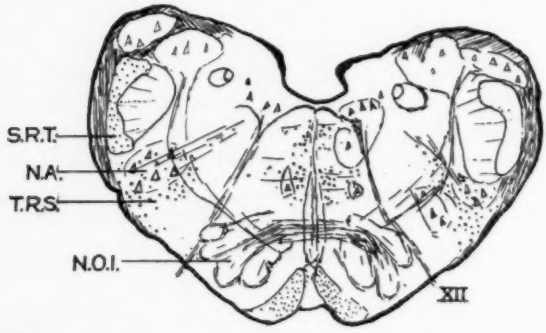

FIG. 15.—Experiment I. Marchi stain. S.R.T., sensory root of trigeminal nerve; degenerated fibres due to section of the nerve; N.A., nucleus ambiguus; T.R.S., rubro-spinal tract; N.O.I., inferior olive.

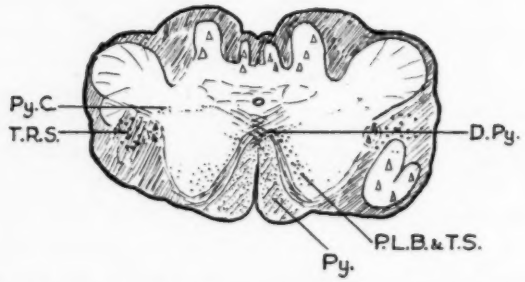

FIG. 16.—Experiment I. Marchi preparation. The degeneration granules of the decussating pyramidal fibres are finer than those of the rubro-spinal tract. It is no longer possible to distinguish tecto-spinal tract from posterior longitudinal bundle. Py., pyramidal tract; Py.C., crossed pyramidal tract; T.R.S., rubro-spinal tract; D.Py., decussation of the pyramids; P.L.B. & T.S., posterior longitudinal bundle and tecto-spinal tracts.

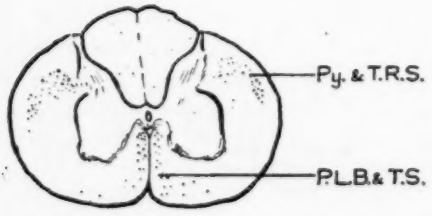

FIG. 17.—Experiment I. Spinal cord at the level of 5th cervical segment. Py. & T.R.S., pyramidal and rubro-spinal tracts; P.L.B. & T.S., posterior longitudinal bundle and tecto-spinal tracts.

FIG. 18.—Experiment I. Section from 6th lumbar spinal segment. Degenerated fibres persist in both ventral and lateral columns.

could not be determined except that there seemed to be an increase in the number of scattered degeneration-granules in the formatio reticularis. In a personal communication Dr. Gordon Holmes has suggested that these fibres may be cortico-bulbar. Further study of this tract is projected with several other possibilities in mind.

(2) Posterior longitudinal bundle presented in the pons a sprinkling of coarse granules near the mid-line. At the top of the medulla they are displaced ventrally by the bundles of entering fibres from the vestibular system. These degenerated fibres pass downwards into the ventral columns of the spinal cord, together with the fibres of the predorsal bundle from which they cannot be distinguished.

(3) Predorsal fibres (presumably tecto-spinal) pass downward from the highest section, on either side of the raphé, only distinguishable from the degenerating fibres in the posterior longitudinal bundle by their more ventral location and their denser grouping. In the cord they are indistinguishable from the posterior longitudinal bundle fibres with which they enter the ventral columns where degeneration-granules are easily followed as far as the lower lumbar segments (figs. 17, 18).

(4) The descending motor fibres or mesencephalic root of the V-nerve were found degenerated from beneath the lateral limits of the fourth ventricle to the middle of the pons, where they turned and passed through the chief sensory nucleus of the V, just lateral to the rubrospinal tract, and joined the trunk of the V-nerve. The sensory root of the V was completely degenerated on the right, due to section of the nerve at the base of the skull, and the degenerated fibres could be followed downward in the spinal root of the V. There was also a small group of degenerated descending fibres in the spinal root of the left V-nerve.

(5) The descending fibres of the rubrospinal tract were replaced by myelin granules about equal in number on the two sides and differing from the pyramidal fibre granules by being coarser than the latter. At the level of the superior olive the rubrospinal tract has moved ventrally and laterally so as to pass in a band around the lateral boundary of the superior olivary nuclei (fig. 14). The fibres then enter the seventh nucleus, which lies immediately below, and are sprinkled out among the cells of this nucleus and its caudal continuation, the nucleus ambiguus (fig. 15). A few of the degenerated fibres pass dorsalwards with the fibres of the seventh nerve-root toward the genu of that nerve, and likewise at a lower level with the dorsally

directed motor fibres of the ninth and tenth nerves from the nucleus ambiguus (fig. 15). The degenerated tract was traced directly down to its characteristic prepyramidal position in the cord.

To summarize the anatomical findings in Experiment 1: There was a small amount of pus about the wax in the cranial cavity. There was, however, no encephalitis of the brain-stem. That the red nuclei did not function after the operation is shown as follows: (1) There was chromatolysis of the caudal end of each red nucleus—the nucleus magnocellularis. (2) The incision A—C appeared microscopically to have cut across Monakow's bundle. (3) The area of hæmorrhagic softening which destroyed the whole of the right side of the brain-stem in the upper pons likewise destroyed the rubrospinal tract on that side (fig. 12). (4) There is a heavy degeneration of the rubro-medullary and rubrospinal tracts, shown by Marchi's method, about equal on the two sides. It is possible to state with certainty, therefore, that all of the mesencephalon and higher centres were removed or without connection with the rest of the organism, except that the hypophysis and its blood supply were intact. The metencephalon, except for the area of hæmorrhagic softening in the upper pons, was intact, and its neurones capable of functioning, as demonstrated by Nissl stains.

FIG. 19.—Experiment XXI.

Animal XXI (p. 221).—Death on the twenty-second day after decerebration. Cause of death, pneumonia, and intracranial infection. The decerebration was complete. All of the cerebrum and basal ganglia were removed, the line of decerebration passing through the middle of the inferior colliculus dorsally to 1 mm. above the upper edge of the pons ventrally. (Line A—B, fig. 19). Brain-stem and segments of cord were stained by the Marchi method. There was degeneration of the corticospinal, rubrospinal, and tectospinal tracts, and the posterior longitudinal bundle. Degenerated fibres were traced into the lowest dorsal segments in the ventral and lateral columns.

Animal II (p. 195).—Death on the twenty-third day after decerebration. Cause of death, accident due to lively running movements. Lungs showed evidence of recent broncho-pneumonia in recovery stage. The level of decerebration was more anterior than in the last one described, passing between the superior and inferior colliculi dorsally. The section was slightly oblique, removing more tissue on the left than on the right. No note was made of the level ventrally, but Marchi sections of the brain-stem and cord showed heavy bilateral degenera-

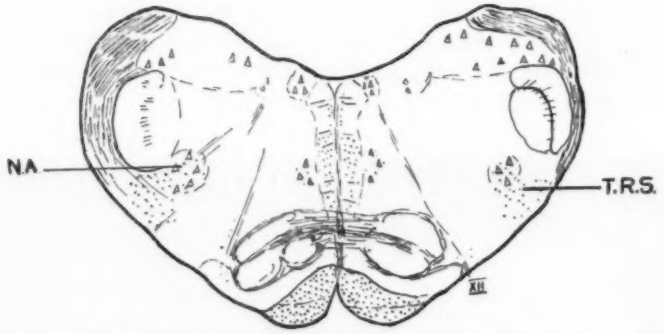

FIG. 20.—Experiment II. Marchi preparation. T.R.S., rubro-spinal tract; N.A., nucleus ambiguus.

FIG. 21.—Experiment IX.

tion of the rubrospinal tract in addition to degeneration of the other descending tracts (see fig. 20). Therefore, most, if not all, of the red nucleus must have been removed. Degenerated tracts were followed down into the lower lumbar segments in the lateral and ventral columns.

Animal IX (p. 203).—Death on the eleventh day after decerebration. Infected hæmatoma beneath wax. The level passed through the superior colliculus dorsally and just in front of the emerging fibres of the third nerve ventrally (line A—B, fig. 21). The time was not

sufficient to provide for complete degeneration, but there were a few black granules shown by the Marchi method in the pyramidal tract and posterior longitudinal bundle, and also the rubrospinal tract. One may assume, therefore, that there was some injury to the red nuclei, unless some of the fibres of Monakow's bundle have a higher origin, e.g., thalamus, as claimed by Bechterew [5].

Animal XVII (p. 218).—Death nine days after decerebration. The level was between the superior and inferior colliculi dorsally. No note was made of the ventral level but some of the hippocampus was left on the right side. Microscopic examination by the Marchi method showed degeneration in all the chief descending tracts, including the rubrospinal. The reaction of degeneration was incomplete, doubtless due to the short time which had elapsed since decerebration.

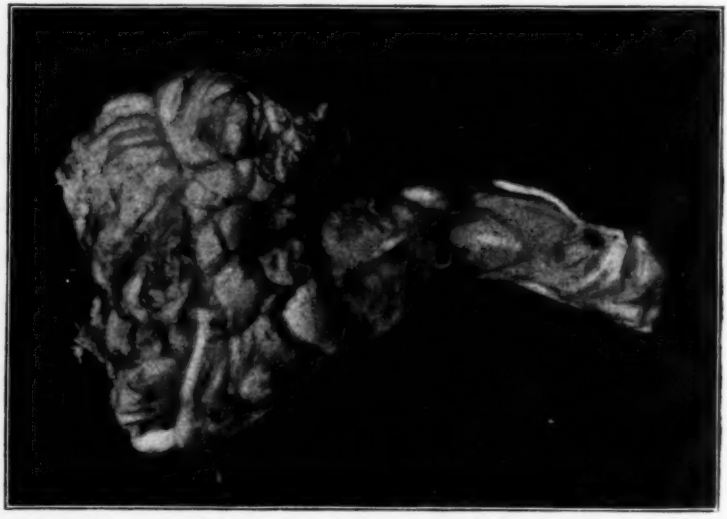

FIG. 22.—Experiment XXIII. The under-surface of the remaining mesencephalon may be seen above the upper margin of the pons.

Animal XXIII (p. 222).—Death five and a half days after decerebration. There was hæmatoma beneath the wax in the cranial cavity. The lungs were congested and there was exudate in the bronchi. The decerebration had been complete. All of the colliculi had been removed and some of the tegmentum caudal to the inferior colliculus. Ventrally, the level of incision was considerably higher, leaving 4 mm. of the left

cerebral peduncle above the pons, and 2 mm. of the right. See photograph of the brain-stem, taken from the left side (fig. 22), also schematic representation of the level (fig. 23). Microscopical sections were made of the top segments, by the Nissl and Loyez methods. There was no encephalitis. The red nuclei were present, at least in part, and may have been functioning.

FIG. 23.—Experiment XXIII.

FIG. 24.—Experiment XXVI.

Animal XXVI (p. 226).—Death three days after decerebration. No cause of death could be ascertained. The decerebration was oblique, the level indicated in fig. 24 by the line A—B for the left side and the line C—D on the right side. Microscopical examination of sections through the top block of the brain-stem showed more of the red nucleus present on the right than the left. Most of the cells of the nucleus magnocellularis showed chromatolysis. The right inferior colliculus was intact. Part of the left inferior colliculus was missing.

Animal VI (p. 201).—Death two days after decerebration. No cause of death determined. The microscopical level of decerebration, which was oblique, is shown in fig. 25, by the line A—B for the left side and C—D

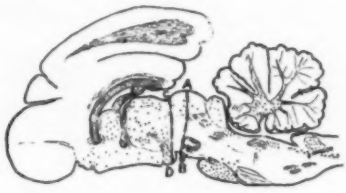

FIG. 25.—Experiment VI.

for the right side. Microscopical sections showed a circumscribed area of hæmorrhage which destroyed most of the left red nucleus and probably all. The cells of the right red nucleus were present. About half of the large cells showed chromatolysis, the rest were normal. There was no infection. Both inferior colliculi were normal and there was no interference with the lateral fillets.

Animal IV (p. 199).—Killed on the sixth day after decerebration. There was evidence of beginning broncho-pneumonia. The decerebration was complete except for a piece of the left crus, which was attached to the pons by a narrow strip of tissue. The pituitary was intact with its blood supply. The macroscopical level of decerebration is shown by line A—B, fig. 26. Microscopically the whole top of the

Fig. 26.—Experiment IV.

brain-stem was softened and infected, except the narrow strip of pyramidal fibres where the piece of cerebral peduncle mentioned above was attached. There was an area of hæmorrhage in the right proximal half of the pons, destroying the formatio reticularis here. There was no encephalitis in the deeper segments of the pons. The cells of the vestibular nuclei and the nuclei of Deiters were for the most part normal, but large cells in the formatio reticularis (called nucleus salivarius superioris by Winkler and Potter [64] all showed chromatolysis, suggesting that their axones had been sectioned. There was no evidence of red nucleus anywhere.

Fig. 27.—Experiment V. Left side.

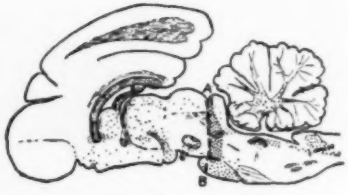

Fig. 28.—Experiment V. Right side.

Animal V (p. 200).—Killed in apparently good condition on the sixth day after decerebration. There was ophthalmia of the right eye and the right V nerve was damaged near its exit from the pons. The level of decerebration as seen microscopically passed through the superior colliculus on the left side (A—B, fig. 27) and between the two colliculi on the right side (A—B, fig. 28).

Ventrally it came below the upper margin of the pons, but there was a small block of tissue attached by some of the fibres of the crura cerebri to the pons. This overlay the pituitary whose blood supply was apparently intact. There was a considerable hæmorrhage extending down into the pons and causing destruction of almost all the normal tissue indicated in the dotted areas of figs. 27 and 28. There was cuffing of the vessels with polymorphs showing that there was some encephalitis of the superficial areas in addition to the softening due to hæmorrhage. Such of the decussation of Meynert and Forel as may have existed was completely destroyed. Careful microscopical examination showed the red nuclei removed or destroyed by hæmorrhage. On the left side the formatio reticularis was destroyed at least as far down as the middle of the pons. On the right a few nerve cells could still be recognized in parts of the upper pons, but they were not normal as shown by Nissl staining. The destruction did not reach as far as Deiters' nucleus.

In this case it is certain that the red nucleus on both sides was completely destroyed. Much of the inferior colliculi was left and microscopically normal, but all connection of these centres with the rest of the brain-stem was severed. The level of decerebration is in reality the middle of the pons.

FIG. 29.—Experiment VII.

Animal VII (p. 202).—Death twenty-eight hours after decerebration, due to hyperpyrexia after warming before stove. No evidence of infection. A small amount of isolated brain tissue remained over the infundibulum. Top of brain-stem was smooth, symmetrical, and convex in outline, beginning in the middle of the inferior colliculi dorsally and the upper border of the pons ventrally. (Fig. 29, line A—B).

To microscopical examination, part of the red nucleus was present on either side and many of the cells were normal. Several small areas of hæmorrhage extended downward a few millimetres. The pons was otherwise normal.

Animal VIII (p. 203).—Death on the seventh day after decerebration due apparently to secondary hæmorrhage from the brain-stem. There was pus and blood-clot between the wax and the brain-stem. Progressive microscopical sections showed that there was no encephalitis below the superficial layers. To microscopic examination the level of decerebration passed between the superior and inferior colliculi on the right and through the middle of the inferior colliculus on the left, to end at the upper border of the pons ventrally. See figs. 30 and 31. A small amount of brain matter remained above the infundibulum. The tissue corresponding to the dotted areas was softened and filled with compound granular corpuscles.

FIG. 30.—Experiment VIII. Right side.

FIG. 31.—Experiment VIII. Left side.

There was no remnant of red nucleus on the left side and only a few cells belonging to this nucleus remained on the other side. The interpeduncular ganglion and most of the substantia nigra cells were normal as well as the pontile nuclei. Most of the formatio reticularis was normal. With the exception of a small proportion of the cells of the right red nucleus, the level of decerebration was below the mesencephalon.

CHAPTER VI.

(*a*) *Decerebrate Rigidity in Chronic Experiments.*

Decerebrate rigidity was first mentioned in experimental animals by Sherrington in 1896 [53]. He described it as a "tonic rigidity in certain groups of skeletal muscles, especially those in the dorsal aspect of the neck, tail, and of the extensor surfaces of the limbs." Decerebrate rigidity in animals is, then, a tonic rigidity of the anti-gravity muscles, the muscles employed in maintaining an erect posture.

The neurogenic source of this phenomenon has been the subject of many studies. Hughlings Jackson [24] had suggested that the cause

of hemiplegic rigidity in clinical cases was due to the "unantagonized influence of the cerebellum" . . . "after the influence of the cerebrum is taken off." Similarly, the decerebrate rigidity of experimental animals has been commonly considered a release phenomenon.

It has been maintained that the red nuclei were the source of the rigidity after decerebration through the mid-brain or after a lesion to the cerebellum. The intimate connection of these twin nuclei with cerebellum, thalamus, globus pallidus, and spinal cord seems to fit it for such a function. Moreover, it has been shown, notably by Graham Brown [9], that electrical stimulation of the red nuclei results in a postural response and the stimulation is followed by a well maintained after-discharge. In a different way, Magnus and his co-workers have demonstrated these postural movements also. They have described a number of position reflexes which may be seen in the decerebrate animal. Many of these position reflexes take place only if the mid-brain including the red nucleus be present. Others continue to be seen after the removal of the mid-brain. But because mid-brain and red nucleus may have to do with position mechanisms, as indicated above, it does not necessarily mean that they are indispensable for the maintenance of extensor rigidity.

The experiments reported in this paper prove that the red nuclei are *not* necessary for the maintenance of decerebrate rigidity. Inasmuch as the animals were kept for long periods of time the possibility of irritation effects disappears. The rigidity must be a release phenomenon. But it is not release of the rubrospinal tract.

Careful microscopical examination, as described above, showed for example that in experiments IV and V there was no red nucleus to be found. In experiment I, cells of the red nucleus were found in a block of tissue which was severed from the brain-stem. Below this the area through which the rubrospinal tract must have passed was completely softened and below this there was heavy degeneration of the rubrospinal tracts. In other experiments (as II, VIII, XVII, XXVI) the greater part of the red nuclei was missing and probably the remnant was not functionally active.

In experiment I, just mentioned, the animal showed extensor rigidity during the early days following operation, and at times this rigidity was seen to vary in intensity during an examination. On the twelfth day after operation it was noted that the right hind-leg was rigid in flexion while the other limbs maintained extensor rigidity. In experiment IV there was extensor rigidity of moderate intensity on the first two days after operation. During the next two days a tendency was noted to assume a rigidly flexed attitude. On removal from the bath to be dried, extreme extensor rigidity appeared with retraction

of the head. This was followed by a short period of tonic flexion of the limbs and extrusion of the fore-claws. There were then several alternations of flexor and extensor rigidity.

Animal V developed extensor rigidity on the day of operation. Next day it was much increased. On the third day the extensor rigidity was marked, especially after the animal had been handled and turned in the bath. The tone was probably sufficient to support the weight of the body with ease. On the sixth day the animal was removed from the bath and dried in the incubator. During the drying process there was no rigidity, the limbs being flaccid. After this one of the nerves was dissected out for a stimulation experiment. During the dissection there were vigorous movements, micturition and the development of extreme extensor rigidity which was maintained during manipulation, but lessened when the animal was left quiet for a quarter of an hour. During further dissection extreme rigidity returned. By reference to p. 251 it will be seen that because of softening, the actual level of decerebration in this animal was the middle of the pons. Preparation VIII developed a considerable extensor rigidity in all four limbs immediately after operation. On the fourth day extreme rigidity was noted in all four limbs, but after the preparation was turned from the right to the left side the right fore-limb went into tonic flexion with extrusion of claws. Many of the position reflexes described by Magnus were later elicited in this preparation. (See p. 203.)

It is unnecessary to multiply examples. Decerebrate rigidity appears even though the red nuclei be removed. The preparations with high decerebrations acted differently, went into violent running movements, and were much more difficult to keep alive than those in which the removal was more posterior. There was perhaps more variability in the posterior removals, and the rigidity is frequently intensified by afferent stimuli. This variability was noted by Cobb, Bailey, and Holtz [11] in acute preparations, as well as the effect of afferent stimulation. Magnus [40] concluded that to remove the mid-brain resulted in the loss of the ability to bring the body to normal from any abnormal position. The difference in the behaviour of the preparation according to the level of decerebration cannot be denied. Whether or not there is any difference between the rigidity of the animals with and those without red nucleus, as suggested by Cobb, Bailey and Holtz, must be decided by myographic examination of the tonus of isolated muscles. To less refined methods of examination the rigidity when present is the same regardless of the fate of the red nuclei.

In a number of the complete decerebration experiments, retraction of the head amounting to opisthotonos appeared in preparations which at the same time showed extreme extensor rigidity and this was

frequently spasmodic. That is, head retraction appeared periodically together with an increase in extensor rigidity. It seems that when extensor rigidity becomes sufficiently intense, opisthotonos usually appears as a part of the same phenomenon, as Wilson [63] has suggested for tonic fits in man.

The term decerebrate rigidity is generally taken to mean extensor rigidity. But in completely decerebrated specimens another type of rigidity sometimes appears, tonic contraction of the muscles on the *flexor* aspect of the limbs. This is associated at times with bending of the head downward and extrusion of the fore-claws. After *semi*-decerebration this phenomenon appeared much more frequently (p. 232), alternating with extensor rigidity as though complementary to it. It would be more accurate, therefore, to speak of extensor and flexor rigidity as two types of decerebrate rigidity. Sherrington, Thiele, and Weed have independently noted the occasional appearance of flexor rigidity.

Study of the results of the more anterior unilateral decerebrations demonstrates that the extensor rigidity may be ipsilateral in the acute preparation, as described by Sherrington, but that after the stage of stimulation disappears the extensor rigidity becomes contralateral in the chronic preparation. Correspondingly, flexor rigidity, though sometimes contralateral at first, quickly becomes ipsilateral. These observations suggest that the fibres whose interruption give rise to extensor rigidity decussate somewhere between the anterior part of the mesencephalon and the upper part of medulla oblongata. This is in agreement with the experiments of Thiele.

The anatomical basis generally accepted for extensor rigidity at present is, very briefly: the rigidity is a proprioceptive reflex depending on the integrity of the local reflex arc, including the afferent and efferent paths to any muscle in question (Sherrington) [56]. The condition appears only after section of the brain as low as the posterior part of the thalamus (Thiele) [57], or the anterior part of the mid-brain (Magnus) [40]. In the chronic experiments of de Barenne there was no rigidity after removing fore-brain, leaving thalamus intact. It would seem that the tract whose interruption is responsible for decerebrate rigidity has its origin about the level of the hypothalamus.

On the other hand, section of the brain-stem below the pons immediately abolishes the rigidity on the ipsilateral side [54], but not on the contralateral side. The phenomenon is therefore independent of the pyramidal tract. The nerve paths responsible for the decere-

brate rigidity, whatever their source may be, are found in the antero-lateral columns of the cord, since cutting the posterior or the ventral columns does not influence rigidity.

There has been considerable discussion as to what is the source of the tonic influence which is brought into play by decerebration. It must be located in the pons or upper medulla oblongata. The action of this centre, or perhaps reflex arc, is modified by stimuli from the otic labyrinth although decerebrate rigidity is not abolished by section of the eighth nerve [54]. There exists an area on the anterior surface of the vermis cerebelli, stimulation of which inhibits decerebrate rigidity [53], [33], [59], [11]. Removal of this area induces this condition if not already present. Rigidity has been observed to continue for some time after total ablation of the cerebellum. Cobb, Baily and Holtz [11] maintain that the inhibitory pathway is the dentate-rubral fibres. Weed believed the cerebellum to play an important rôle in the cause of decerebrate rigidity, but the removal of the cerebellum in his experiments did not abolish it immediately. Thiele [57] reported that progressive removal of slices of the cerebellum induced decerebrate rigidity until the vicinity of Deiters' nucleus was reached, when all rigidity suddenly disappeared. This author likewise made progressive sections down the brain-stem and reported that the decerebrate rigidity which appeared when the section passed below the posterior end of the thalamus, disappeared suddenly on reaching the level of Deiters' nucleus. These were acute not chronic experiments. Magnus considers that the decerebration must be as low as the anterior part of the mid-brain before rigidity results. He describes decerebrate rigidity as a caricature of standing, inasmuch as the ability to assume and maintain an upright position disappeared with the removal of the mid-brain [40]. Magnus likewise agrees that decerebrate rigidity may persist until the level of removal reaches the lower margin of the pons.

It has been shown that the mid-brain and pons of a decerebrate preparation can be bisected in the sagittal plane without loss of decerebrate rigidity. On one occasion we confirmed this, as follows:—

A complete decerebration was performed on a cat at 11 o'clock in the morning. The level was between the colliculi dorsally and 3 mm. in front of of the anterior margin of the pons ventrally. The extensor rigidity was well maintained and the preparation would stand if properly adjusted on its feet. At 4.45 p.m. a sagittal mid-line incision was made through mid-brain, pons and well down into medulla oblongata. The rigidity continued and was still in evidence at 6.15 p.m. By this time the rigidity was less intense and the

respiration was just coming to a stop. The lungs were artificially ventilated. The limbs, after a stage of clonus, improved their extensor rigidity for a time.

Examination of the brain-stem showed the longitudinal section to be complete at the level of the red nuclei. At the level of the upper medulla the the bisection was complete dorsally but stopped 1 or 2 mm. short of the ventral surface, only severing a part of the inter-olivary body. In the lower medulla a considerable hæmorrhage had occurred which may have been responsible for the respiratory failure.

As the rubrospinal tract decussates almost completely in the mid-line, this is added evidence that the presence of the red nuclei is not essential to the existence of decerebrate rigidity. The experiment likewise suggests that paths which are responsible for decerebrate rigidity do not decussate in the medulla.

Nothing has been encountered in these experiments which would contradict the view of Thiele that the integrity of Deiters' nucleus is essential for the production of decerebrate rigidity, or that the spinal fibres arising in Deiters' nucleus carry efferent impulses indispensable to the reflex. Weed suggests that the ventral cerebellar tract of Gowers carries afferent impulses in the reflex circuit, which is responsible for the rigidity. This tract passes dorsally below the level of even the lower decerebrations and was seen to be intact in all of our anatomical preparations that were carefully studied.

(*b*) *Temperature Control.*

The whole literature on the subject of temperature control and the nervous mechanisms which are concerned has been so carefully reviewed recently by Barbour [1] that no attempt need be made here to give any detailed account, and reference may only be made briefly to such papers as bear most closely on the results here reported.

It has been shown by Rogers [50] that in pigeons section of the brain-stem below the level of the thalamus completely removes all temperature control, while section above the thalamus does not, so that even in birds, in which the development of the corpus striatum is very different from that of mammals, section of the brain-stem in the region we have studied destroys all temperature control. The similarity with the results obtained in cats is the more marked when the experiments of de Barenne [2] [7] are also taken into consideration. He removed practically all the brain above the thalamus in the second of the two cats described in the above paper, and yet found it to have a normal temperature control. Therefore, in cats also the control of temperature

may be definitely located between the level of the middle of the superior colliculi and 2 mm. in front of the pons below and the upper limit of the thalamus above. Such a situation for the centres controlling temperature regulation is in entire accord with the work of Barbour on the effect of localized heating of the brain.

Isenschmidt and Krehl [22] in 1912 showed that rabbits in which the brain-stem was divided at the level of the junction of the diencephalon and mesencephalon lost all power of temperature control, while if the hemispheres alone were removed control was not lost. But their animals without temperature control only survived a few days, and considering how long reactions may be depressed following a lesion, the possibility of a later return of temperature control was not excluded.

Later Isenschmidt and Schnitzler [23] made various sections in the mid-brain at different levels, these sections being often one-sided and partial, and they came to the conclusion that the heat regulation centre was in the region of the tuber cinereum. This would be consistent with our results, but their conclusions cannot be regarded as firmly established since again they were unable to keep alive for more than a few days any animals which lost their power of temperature control. Consequently they could not elaborate their results by examination for nerve degeneration. The "Zwischenhirnstich" of Leschke [31] gave similar results.

The animals that we report offer therefore strong confirmatory evidence as to the position of the centres controlling temperature, and it should be much easier to determine whether these are in the thalamus or tuber cinereum by the employment of the methods we have developed for nursing animals which have lost their power of temperature regulation.

It will be evident from the experiments that have been described that no sign of temperature control remains and that no such control returns at any rate within two weeks. The complete absence of shivering in the bilaterally operated animals and its ready occurrence after the unilateral operation is very striking, and it is of considerable interest that in the latter case shivering occurs equally on the two sides of the body. With the unilateral decerebrations it was noticed that if the remaining brain matter was exposed to some pressure (as occurred when wax was used in these cases) the raised intracranial pressure readily destroyed the power of temperature control, and it was also noticed that in the other animals which showed deficiency of temperature control the lesion had slightly damaged the left side of the brain-stem as well as the right.

It seems probable, therefore, that tracts which carry either sensory or motor fibres intimately concerned in temperature control run in the mid-brain close to the mid-line, possibly for instance in the posterior longitudinal bundle, though we have no direct evidence of this.

The animals with bilateral decerebration showed a considerable change in the respiratory rate with change in body temperature in spite of the apparent absence of temperature control. This however appears to be adequately explained by assuming that a rise in body temperature alters the respiratory rate by affecting the respiratory centre directly, just as it alters the heart rate by direct action on the heart, and that the respiratory rate may be still further quickened by the indirect action of a metabolism which has also been increased as the result of the raised body temperature. In any case the quickening of the respiratory rate with raised body temperature is probably considerably less than that occurring in the intact animal [20] [30] [48].

While up to the present these preparations have given no great additions to our knowledge of the mechanisms concerned in temperature control, the possibility of the preservation over long periods of animals, in which this control has been lost, would seem to offer many new opportunities for the investigation of this problem.

Conclusions.

(1) A technique is described which allows cats in which all the brain above the level of the pons has been completely removed to be preserved for days and occasionally as long as three weeks. The essential factor is shown to be the maintenance artificially of a normal body temperature.

(2) Chronic decerebrate preparations obtained in this way are found to maintain throughout this period the general characteristics described by Sherrington. The extensor rigidity is usually maintained with brief intermissions, and further proof is thus offered that it is a "release phenomenon." Rigidity continues in many cases after full degeneration of the divided tracts has occurred.

(3) Decerebrate rigidity is described lasting for more than two weeks in animals in which all the red nuclei can be shown histologically to be no longer functioning. Decerebrate rigidity can therefore occur in the absence of the red nucleus, and although many reactions and position-reflexes disappear in the more posterior decerebrations, the character of the extensor rigidity seems to be the same. It was

sometimes found that sensory stimuli would increase the rigidity already present, or cause it to reappear if it were absent.

(4) Decerebrate rigidity is probably dependent on some centre or reflex arc at about the level of Deiters' nucleus. None of our histological examinations showed any lesion to this nucleus nor to the ventral spino-cerebellar tract of Gowers, and the rigidity did not disappear after mid-line sagittal section of the pons and medulla.

(5) Head retraction accompanies extreme rigidity, but is only seen with other evidences of an irritative lesion such as may be produced by progressive hæmorrhage. It then forms a part of what may be called a tonic extensor fit which on the day of operation occasionally developed into a well marked opisthotonos. Spontaneous nystagmus sometimes appears also as the result of this irritation.

(6) The level of the section was generally rather oblique and usually more was removed on the left side; many animals showed an asymmetric head position, usually with a tendency to bend it to the left side. In these animals the section level suggested a possibility of some of the right red nucleus cells still functioning.

(7) Certain differences between the acute and chronic states were noticed. In the later stages there is a much greater tendency for flexed positions to be assumed, and these are often asymmetrical and sometimes flaccid and sometimes rigid. Of these rigid flexion of the terminal joints of the fore-limbs with extrusion of the claws is very common.

(8) The preparations show no sign of temperature control and never shiver. Bilateral shivering is however seen after unilateral decerebration where temperature regulation is preserved. Variations in the respiratory rate are seen after bilateral decerebration as the result of differences in body temperature, but these variations are probably not so great as in the intact animal.

(9) The respiratory rate is usually that normal for a cat, i.e., about 24. Normal respirations have been observed for days even when the section was at the lower margin of the inferior colliculi.

(10) Pseudaffective reflexes were usually much more developed after the first few days than immediately after operation, and new responses were seen. Besides those described in the succeeding section, movements of the head away from certain nocuous stimuli were noticed and occasionally a movement of the fore-limbs as though directed to the protection of the head.

(11) Vocalization was noted in ten of the 124 complete decerebra-

tions. This was rarely seen except after three or four days, and consisted most commonly in purring after the stomach had been filled with milk by a stomach tube. When purring was observed the animal was a kitten or a young female. Other cats growled, such sounds being never repeated, and in this case the sounds were only observed in old males. A true mew has only been observed in one animal which made such a sound on two occasions, but would not do so in response to nocuous stimuli. An ill co-ordinated cry, resembling the sound a cat may make while anæsthetized, has been observed in five animals, but it too is apparently sporadic and is rarely repeated.

(12) Many preparations show a well developed mastication reflex with chewing of the food (or tube), swallowing of the bolus and with a final nose and mouth-licking reflex. This may be initiated by mere opening of the mouth sometimes or by insertion of food into the back of the mouth. A stomach tube is merely swallowed during the first day, is often also chewed later, while after four or five days food may be well swallowed while a stomach tube is received with apparent objection, the head being moved about and attempts being made to spit it out.

(13) Movements are seen in animals with a section between the superior and inferior colliculi and these increase after the first few days. They consist of movements as described under (10) and (14), and also of spontaneous progression movements and of kicking when touched. They were distinct from the violent movement found with more anterior sections (already described by others). It has not so far proved possible to preserve animals for any time when the section has been at the level of the anterior border of superior colliculi, owing to the complications introduced by these violent reactions.

(14) Acoustic reflexes become more brisk after the first few days. Lifting of the head to one side (usually the left) has been often seen, and would sometimes occur in reaction to such slight sounds as were made for instance by entering the room quietly, and this in spite of the fact that the bath stirrer was maintaining a constant noise. Though the constant noise gave no reaction, it caused a reaction when the motor was started after a quiet interval.

(15) Glycosuria persisting for some time after decerebration (as described by J. Mellanby) is confirmed, but this glycosuria disappears again on the second or third day and does not reappear. The cessation of glycosuria is not caused by disappearance of glycogen.

(16) Unilateral decerebration was carried out on a series of seventeen

cats, the removal extending back to the level of the pons in some, to the anterior part of the mid-brain in others.

(17) In these semi-decerebrate animals forced movements were always directed away from the side of removal. The head was rotated with occiput away from the side of removal and the neck flexed and retracted so as to carry the head over to the sound side. In some of the more anterior removals a transient stage of forced movements to the ipsilateral side followed operation, to be succeeded invariably by the opposite.

(18) In experiments in which the semi-decerebration passed through the anterior part of the mesencephalon, extensor rigidity was found in the contralateral limbs. This was preceded sometimes by ipsilateral or bilateral extensor rigidity. When the semi-decerebration was more posterior and passed between mid-brain and pons, there was considerable variation in the rigidities and a tendency for them to be asymmetrical. The anatomical deduction is that the pathway whose interruption is responsible for extensor rigidity decussates in the mid-brain.

(19) A condition of increased resistance of the flexor muscles to passive extension was described, both in complete decerebrations and semi-decerebrations. In the latter, when the removal was anterior, this flexor rigidity appeared usually in the ipsilateral limbs, though it might be seen in the contralateral limbs for a short time after operation. Thus it alternated with extensor rigidity.

(20) Flexor rigidity as an entity may be described as tonic innervation of those muscles which are subjected to tonic inhibition during extensor rigidity. It is possible to speak of two types of decerebrate rigidity.

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THE PATHOGENESIS OF SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD, WITH SPECIAL REFERENCE TO ITS CONNECTION WITH ADDISON'S (PERNICIOUS) ANÆMIA, ACHLORHYDRIA AND INTESTINAL INFECTION.

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AND

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SUBACUTE combined degeneration of the spinal cord has in the past been chiefly investigated by neurologists, who were only interested in a minor degree in the associated anæmia. On the other hand, the spinal changes observed in Addison's anæmia have been investigated chiefly by physicians, whose interest was in the anæmia rather than the spinal disease. The present paper is an attempt to discuss the two groups of cases from a common standpoint, and to show that both depend upon the same underlying pathological processes—oral sepsis, absence of free hydrochloric acid from the stomach contents throughout digestion, and consequent intestinal infection and intoxication.

The term Addison's anæmia is used in this paper instead of pernicious anæmia. Addison [1] first described the disease in 1847 and called it "idiopathic anæmia." Twenty years later Biermer published his work on the same subject and called the disease "pernicious anæmia." But beyond the pernicious name he invented, Biermer added little but confusion to our knowledge of the subject, and as the disease is neither idiopathic nor necessarily pernicious, there can be no doubt that "Addison's anæmia" is the most satisfactory name.

I.—THE PATHOGENESIS OF ADDISON'S ANÆMIA AND ACHLORHYDRIA.

Before considering the pathogenesis of subacute combined degeneration of the spinal cord, it is necessary to summarize the views we hold as a result of recent investigations on Addison's anæmia, particularly with regard to its association with achlorhydria. For the following

reasons we believe that the achlorhydria is an essential predisposing cause of the anæmia.

(1) There is abundant evidence that the achlorhydria precedes the development of the anæmia. As Robert Hutchison first pointed out in 1900, there is generally a more or less long history of digestive disturbances, of the type commonly associated with achlorhydria, preceding the first symptoms of anæmia. In one case achlorhydria was actually discovered twelve, in another ten, in another three years, and in another one year before the onset of anæmia.

(2) In sixty-four out of sixty-six fractional test meals carried out at Guy's and the London Hospitals on cases of Addison's anæmia complete achlorhydria occurred throughout the period of digestion. At whatever stage in the development of the anæmia the examination is made achlorhydria is found. It was present, for example, in cases in which the hæmoglobin percentage had not fallen below 85, 85, 80 and 68; it is thus a far more constant symptom than any other, even than the hæmatological signs, such as a high colour index and the presence of megaloblasts, as these are often absent in the early stages and even temporarily when the anæmia is severe.

(3) It persists when the anæmia has almost disappeared, either spontaneously or as a result of treatment. Thus in four cases it was still present when the hæmoglobin percentage was 85, 82, 80 and 70 respectively, compared with 45, 38, 23 and 53 respectively some months or years before.

(4) There is no constant change in the curve of secretion in any form of anæmia, except Addison's. Thus fractional test meals in our last four patients with gastric or duodenal ulcer, complicated by severe secondary anæmia due to hæmorrhage, gave curves of exactly the same form as would have been expected in the absence of hæmorrhage; the percentage of hæmoglobin in these cases was 30, 33, 48 and 49, which is quite as low as one would expect to find in an average series of cases of Addison's anæmia when first examined. In two cases of secondary anæmia caused by rectal hæmorrhage with a hæmoglobin percentage of 44 and 42 respectively, and in two cases of chlorosis with a percentage of 25 and 48, the curves of gastric secretion were normal. It is obvious, therefore, that anæmia does not cause achlorhydria.

(5) In a long series of cases it becomes clear that the achlorhydria is not specific, but that whatever its origin may be, it predisposes to the development of Addison's anæmia. Bennett and Ryle [5] have shown that about 4 per cent. of normal young men have achlorhydria. The history

in many cases of Addison's anæmia points to the achlorhydria being of this congenital type. In one it was due to alcoholic gastritis, in another it resulted from a gastro-enterostomy for ulcer, and—what proves conclusively that it is primary and not secondary—in at least five cases Addison's anæmia followed the artificial achylia produced by total gastrectomy performed for cancer. There is thus no constant pathological change, such as atrophy, in the gastric mucous membrane after death, and in one case of Addison's anæmia, in which a fragment was excised during an operation for appendicitis, Dr. R. D. Passey found no atrophy and no more inflammation than in a specimen obtained under similar circumstances in a case of "benign" achlorhydria.

For the above reasons we believe that Addison's anæmia only develops in individuals who have achlorhydria. The anæmia is caused by hæmolytic toxin absorbed from the intestine, where they have been produced by the action of bacteria coming originally from the mouth, the presence of achlorhydria having deprived the stomach of its antiseptic powers, which normally exert a powerful influence in protecting the bowel from such infection.

II.—Degeneration of the Spinal Cord in Addison's Anæmia.

Lichtheim [13] in 1887 described three cases of "pernicious anæmia" with spinal symptoms. A post-mortem performed on two of them showed degeneration of the posterior columns and to a less extent in the lateral columns. His clinical and pathological observations were soon confirmed by Minnich [15] and Nonne [18]; the latter author before long came to the conclusion that his original idea that the degeneration of the spinal cord was secondary to the anæmia must be incorrect and that both conditions were the result of some chronic intoxication.

In the last twenty-five years spinal cord symptoms have been recognized in Addison's anæmia with increasing frequency as they have become more systematically looked for. In 1902 McCrae [14] found them in 25 per cent. of forty cases; in 1918 Woltmann [21] found "indisputable evidence of the destruction of nervous parenchyma" in 80·6 per cent. of 150 cases, which were subjected to a detailed neurological examination at the Mayo Clinic. This corresponds closely with the figures obtained by Minnich [15] [16], who discovered degenerative changes in 77 per cent. of the spinal cords of a consecutive series of fatal cases of "pernicious anæmia."

Mitchell Clarke [17] in 1904 concluded from a study of the literature and from his own cases that the changes in the nervous system in Addison's anæmia could be clearly distinguished from subacute combined degeneration of the cord, whether or not the latter was accompanied by anæmia. We agree, however, with the view expressed by Barker [2] in 1919 that no definite line can be drawn between Addison's anæmia accompanied by changes in the spinal cord, and subacute combined degeneration of the cord accompanied by anæmia. The difference is simply one of degree, and depends upon whether a hæmolysin or a neuro-toxin is the more active. If either toxin is at first produced alone, there is more time for it to give rise to marked changes; thus when Addison's anæmia is severe and rapidly fatal, there may be no time for any nervous symptoms to develop, or, if they do develop, they may be trivial in comparison with those observed in cases in which the nervous degeneration has progressed for many months without any anæmia. There appears to be no essential difference between the clinical symptoms or the pathological changes in the spinal cord except in their severity, whether the nervous degeneration or the anæmia predominates.

III.—Nature of the Anæmia associated with Subacute Combined Degeneration of the Spinal Cord.

In some of the nine cases described by Risien Russell, Batten and Collier [20] in 1900 no anæmia was present throughout the disease; in others it developed towards the end, whilst in others it was an "obtrusive symptom from the first and preceded the manifestation of nervous symptoms by many months." They definitely state that repeated examinations of the blood "failed to reveal the alterations found in pernicious anæmia," the changes being those characteristic of secondary anæmia. The red corpuscles were generally normal in shape, nucleated cells were only found in one case in very small numbers, and no megaloblasts or microblasts were present.

In 1904, Mitchell Clarke [17] from a study of five cases of spinal cord degeneration in anæmia concluded that it is by "no means only, nor even most often, that the form of anæmia is pernicious anæmia."

In an article on subacute combined degeneration of the spinal cord published in 1910, Collier [10] states that "severe secondary anæmia" is almost invariably present at some period of the disease, though its development is sometimes deferred till the last stages. But though he

regarded the anæmia as "definitely secondary," his description of the blood corresponds more closely to that of Addison's anæmia. "The colour index is usually above normal . . . Anisocytosis, poikilocytosis, and polychromatophilia are common. Normoblasts are sometimes numerous." He adds, however, that "megaloblasts have not been found, and the reaction for free iron in the liver has not been obtained in any case," but he makes the important observation that the skin not infrequently assumes a striking lemon-yellow colour.

In the same year Byrom Bramwell [7] described a case in which the nervous symptoms developed three years before the anæmia was obvious, but the blood finally presented all the typical features of Addison's anæmia. Post-mortem excess of iron was present in the liver, and there was a great increase in the red bone marrow; the spinal cord changes were typical of subacute combined degeneration. In 1915 [8] he brought forward further evidence pointing to the anæmia being of the Addisonian variety in subacute combined degeneration of the cord, even when it did not first conform to type. He quotes a case in which rapid changes occurred in the blood during the last fortnight of life, the colour index slowly rising in consecutive investigations from 0·8 to 2·3.

Single cases of subacute combined degeneration of the cord have been described by Taylor and Waterman (1903), Collins (1904), Loudon (1913), and Redwood (1920), and two cases each by Grinker (1908), and Hassin (1917), in which the anæmia was definitely of the Addisonian type. Cadwalader, describing nine cases in 1916, stated his belief that subacute combined degeneration was not associated with any form of anæmia except "pernicious" anæmia.

In his latest article on the subject, published in 1921, Collier [11] came to conclusions entirely different from those in his earlier writings. He states that a careful investigation of the blood changes at various stages of the disease and of the post-mortem findings in a large series of cases, has proved beyond any possible doubt that the blood-changes in every case are identical with those that are met with in the various stages of pernicious anæmia, and that a typical post-mortem picture of pernicious anæmia occurs frequently enough in subacute combined degeneration. In contradiction to his earlier papers he says that "megaloblasts may be found in numbers."

Addison's anæmia, particularly in the early stages and during the periods of remission, may present a blood-picture far removed from what is considered to be typical of the disease. This has been recorded fre-

quently and is the experience of all clinicians. A recent case of undoubted Addison's anæmia, in which numerous blood examinations were made and the diagnosis was confirmed post mortem, illustrates this point clearly (Table I).

TABLE I.—VARIATIONS IN COLOUR-INDEX IN A TYPICAL CASE OF ADDISON'S ANÆMIA.

Date	Red blood corpuscles per c.mm.	Hæmoglobin percentage	Colour index
22.9.21	2,200 000	30	0·7
8.10.21	1,500,000	20	0·6
1.11.21	2,800,000	40	0·7
11.11.21	2,400,000	48	1·2
18.11.21	2,088,000	58	1·4
5.12.21	3,100,000	62	1·0
20.1.22	1,600,000	40	1·25
10.4.22	2,400,000	40	0·8
15.5.22	2,240,000	60	1·3
12.6.22	1,640.000	46	1·4
26.6.22	2,440,000	50	1·0

TABLE II.—BLOOD EXAMINATIONS IN EIGHT CASES OF SUBACUTE COMBINED DEGENERATION OF THE CORD.

Name	Age	Date	Red cells per c.mm.	Hæmoglobin percentage	Colour index	Poikilocytosis	Anisocytosis	Normoblasts	Megaloblasts	Leucocytes per c.mm.	Wassermann reaction
John B. ..	62	12.7.20	2,650,000	66	1·2	+	+	—	—	3,750	Negative
Wm. B. ..	72	—2.22	2,710,000	48	0·88	+	?	—	—	7,000	Negative
		27.6.22	3,200,000	85	1·3	+	+	+	—	5,090	
Thos. M. ..	65	2.3.22	3,500,000	68	0·97	+	+	—	—	9,500	Negative
		27.4.22	4,580,000	68	0·6						
		29.5 22	4,700,000	62	0·65						
		26.7.22	6,150,000	86	0·7						
Edith J. ..	40	30.3.22	3,300,000	58	0·88	—	+	—	—	7,100	Positive (C.S.F. negative)
J. E. W. (male)	52	14.7.19	2,300,000	52	1·1	++	++	+	+		
		29.7.19	1,500,000	54	1·8	++	++	+	+	2,800	
		16.9.19	3,200.000	94	1·5	?	?	+	+		Negative
		3.3.21	3,400,000	70	1·0	+	+	+	—	6,000	
		—3.21	3,140,000	88	1·3	+	+	—	—	3,700	
Margaret H.	64	—2.22	2,860,000	85	1·5	+	+	—	—	?	Negative
Harriet G.	51	—7.22	4,710,000	56	0·6	+	+	—	—	5,800	Negative
Marion H.	42	—7.22	2,380,000	56	1·2	+	+	—	—	7,920	Negative

It would thus appear probable that many of the cases of subacute combined degeneration recorded, including the nine published by Risien

Russell, Batten and Collier in 1900, in which the blood-picture was not characteristic of Addison's anæmia, were none the less associated with Addison's anæmia. The lemon-yellow colour, which Collier observed in many cases before he came to the conclusion that the anæmia was of the "pernicious" type, is quite characteristic of the latter, and, being caused by staining of the subcutaneous fat with pigment derived from hæmoglobin, it affords just as good evidence of hæmolysis as the Prussian-blue reaction obtained in the liver and sometimes in other organs after death. This reaction, although present in almost all cases of typical Addison's anæmia, is sometimes absent in cases of subacute combined degeneration, because the blood destruction has not been sufficiently severe and prolonged.

During the time our present series of eight cases of subacute combined degeneration of the cord was under observation the blood-picture was not typical of Addison's anæmia, but it was quite compatible with an early stage of that condition, and in those cases in which repeated examinations were made the colour index was at times over one, and the film at times showed the characteristic features (Table II).

IV.—Digestive Symptoms preceding and accompanying the Nervous Symptoms of Subacute Combined Degeneration of the Cord.

In 1908 Grinker [12] drew attention to the occasional association of digestive symptoms with subacute combined degeneration of the cord and laid special stress on the frequency of diarrhœa. In 1910 Collier [10] stated that he had occasionally observed symptoms of gastro-enteritis and colitis in the disease. In the same year Farquhar Buzzard [9] stated that gastro-intestinal disturbances may precede or accompany the earliest signs of the nervous disease. In his latest contribution to the subject in 1921, Collier says that in a considerable number of cases symptoms pointing to gastro-intestinal infection, such as vomiting, diarrhœa, anorexia or constipation, were prominent before the onset of nervous symptoms.

In seven of our eight cases digestive symptoms were present. Two patients had had attacks of diarrhœa shortly before the first nervous symptoms appeared; one of these had been actually admitted into hospital on this account. In another case "bilious attacks" with occasional vomiting and attacks of flatulent dyspepsia preceded the nervous symptoms, and in a fourth there was a long history of slight

flatulent dyspepsia. In three others the digestive symptoms only appeared after the first signs of nervous disease.

The digestive symptoms, which are so frequently associated with subacute combined degeneration of the cord, are all symptoms which are often caused by achlorhydria apart from this nervous disease and apart from Addison's anæmia, and which are generally controlled without difficulty by the administration of dilute hydrochloric acid. As these symptoms frequently precede the development of the nervous manifestations, just as similar digestive symptoms frequently precede the development of Addison's anæmia, it seems probable that the achlorhydria precedes the development of the nervous symptoms. It is certainly not due to the anæmia, as the degree of this is generally slight, quite apart from the fact that it is exceedingly doubtful whether anæmia ever does give rise to achlorhydria. The fact that digestive symptoms do not always precede the development of nervous symptoms does not make it any the less likely that achlorhydria always precedes them, as the latter condition may be present for years without giving rise to the slightest indigestion, and it is indeed present in about four per cent. of normal young men without digestive symptoms.

V.—Achlorhydria in Subacute Combined Degeneration of the Cord.

We have had the opportunity of investigating eight cases of typical subacute combined degeneration of the cord by the fractional method of gastric analysis. In all of the eight free hydrochloric acid was completely absent throughout the period of digestion. The test was repeated in three of the cases with the same result.

So far as we know no other cases have been investigated in this way. Llewellys Barker [2] found complete achlorhydria in two cases, presumably after an ordinary one-hour test-meal. In one the anæmia at the time of the examination was said to be "quite definitely not pernicious," though the colour index was 1·1, and in the other the red corpuscles numbered 4,000,000 per cm., the hæmoglobin percentage being 90. Barker's observation is valuable confirmation of our results, but the fact that achlorhydria persists throughout digestion is of course of greater significance than the absence of free hydrochloric acid from the contents of the stomach removed in the ordinary way one hour after the meal has been taken. Dr. J. F. Wilkinson, of Melbourne, informs us that he discovered achlorhydria in a patient who consulted

him for digestive symptoms a year before the first signs of subacute combined degeneration of the cord appeared.

For purposes of control gastric analyses were made in a series of typical cases of disseminated sclerosis and tabes dorsalis. In eight consecutive cases of disseminated sclerosis achlorhydria was never found, the curves of acidity being the same as would be likely to occur in a series of eight normal people. Of nine consecutive cases of tabes dorsalis one was found to have achlorhydria; the remainder had curves which fell within normal limits, though in two cases it was somewhat high. As 4 per cent. of normal individuals have achlorhydria, the single case in this series is probably of no importance (Table III).

TABLE III.—RELATIVE FREQUENCY OF ACHLORHYDRIA IN VARIOUS CONDITIONS.

	Number of cases	Achlorhydria		Low acidity	"Normal" acidity	High acidity
		Number	Percentage			
Normal (Bennett and Ryle) [5]	100	4	4	1	87	8
Various medical diseases (Bell) [3]	425	63	14·8	53 (12·5 per cent.)	205 (48·3 per cent.)	104 (24·4 per cent.)
Addison's (pernicious) anæmia	66	64	96	1	1	0
Carcinoma of stomach	10	3	33	3	3	0
Subacute combined degeneration of cord	8	8	100	0	0	0
Tabes dorsalis ..	9	1	11	1	5	2
Disseminated sclerosis	8	0	0	1	7	0

Gastric analysis may therefore give information of real help in diagnosis, the presence of free hydrochloric acid in any fraction of a test-meal being probably a decisive point against the diagnosis of subacute combined degeneration, whereas the discovery of achlorhydria would considerably strengthen the probability of such a diagnosis being correct. In three recent cases, which presented features very suggestive of subacute combined degeneration, a normal curve of gastric acidity was discovered. Each eventually proved to be a case of syphilitic disease of the spinal cord. These cases are analogous with two others, the only cases in Guy's Hospital in which a diagnosis of Addison's anæmia had been made in spite of the fact that free hydrochloric acid was present in the stomach. At the post-mortem no evidence of hæmolysis was present, one being found to have infective endocarditis, and the

other, who died of lobar pneumonia, having microscopical changes in the spleen, which were typical of Hodgkin's disease.

VI.—Oral Sepsis.

The importance of oral sepsis in Addison's anæmia has been almost universally acknowledged since Hunter first drew attention to the subject over twenty years ago. In his article on subacute combined degeneration of the cord, published in 1910, Collier states that septic gingivitis and stomatitis are common in the disease. One of our eight patients had had all his teeth taken out on account of severe pyorrhœa shortly before we saw him. Two others had had all removed twenty or more years earlier because they were becoming loose. The remaining five had more or less severe gingivitis with pyorrhœa and septic stumps. Only one patient complained of soreness of the tongue; it was abnormally red and corrugated, but there was no ulceration. In another the tongue was abnormally smooth and shiny, the papillæ having atrophied to a great extent, although the patient, who was edentulous, was unaware that she had ever had glossitis.

VII.—The Evidence of Intestinal Infection in Subacute Combined Degeneration of the Cord and Addison's Anæmia.

Streptococci are almost invariably present in the sockets of septic teeth, whether the individual is otherwise healthy or not, but so far as our observations go the *Streptococcus longus* is not often found in the contents of the duodenum removed during life with an Einhorn tube, except in Addison's anæmia and in subacute combined degeneration of the cord. In four normal individuals and in eight cases of infective jaundice from Gallipoli investigated by one of us (A. F. H.) with C. J. Martin in Lemnos in the autumn of 1915 no streptococci were present. Among fourteen patients suffering from various medical conditions the duodenal contents contained the *S. longus* in only three instances, one being in a patient with diabetes and slight pyorrhœa alveolaris, and the other two men with cholecystitis, one of whom also had a severe infection of his tonsils; in all three cases the gastric secretion was normal. In four of the fourteen cases achlorhydria was present, together with very severe oral sepsis in two and slight pyorrhœa in a third, but in spite of this no streptococci were found. In every one of the seven cases of Addison's anæmia and the four cases of subacute combined degeneration of the cord which we have investigated

the *S. longus* was found on microscopic examination and was obtained on cultivation of the duodenal contents. (Table IV.)

TABLE IV.—*Streptococcus longus* IN THE DUODENAL CONTENTS.

	Number of cases	*S. longus* present	Percentage
Normal	4	0	11·5
Infective jaundice	8	0	
Various medical cases	14	3	
Addison's anæmia	7	7	100
Subacute combined degeneration of the cord	4	4	

In spite of the somewhat smaller number of cases, the contrast between the 11·5 per cent. of controls, in which streptococci were found, with 100 per cent. of subacute combined degeneration of the cord and Addison's anæmia, is so striking that the conclusion can probably be drawn that an infection of the intestine with a *S. longus* is an essential factor in the production of these diseases. In any case the presence of the *S. longus* in the duodenum is evidence of active infection of the intestine. In one of our patients an autogenous vaccine made from the *S. longus* isolated from the socket of an infected tooth gave rise to a temporary aggravation of the sensation of pins and needles in the hands and feet each time it was injected.

VIII.—DISEASES OTHER THAN ADDISON'S ANÆMIA WHICH MAY BE ASSOCIATED WITH SUBACUTE COMBINED DEGENERATION.

Schultze, Nonne and Geitlin are said to have reported cases of subacute combined degeneration of the cord, in which the blood picture was that of lymphatic leukæmia, and Collier refers to a similar case observed by Greenfield. I only know of two cases of lymphatic leukæmia in which a fractional test meal has been carried out. In one of these complete achlorhydria was present, but in the other the curve was normal. It is obvious that no conclusions can be drawn from the two cases, but the presence of achlorhydria in one of them would suggest that in leukæmia the oral sepsis and achlorhydria, which are the necessary conditions for the development of Addison's anæmia and subacute combined degeneration of the cord, may be present. This would explain the occurrence of cases of so-called "leukanæmia," in which the blood picture is a combination of leukæmia and Addison's anæmia, as well as those rare cases of subacute combined degeneration of the cord with leukæmia which have just been mentioned.

It is also said that severe cachexia may be associated with similar changes in the spinal cord, but we have been able to find no detailed description of such cases, the majority of which appear to have been

due to cancer of the stomach. In 30 per cent. of our cases of gastric cancer complete achloryhdria was found with the fractional test meal, and oral sepsis is of course not uncommon. Severe anæmia is more common in cancer of the stomach than in cancer elsewhere. This may be due to the fact that a hæmolytic toxin is sometimes produced when achlorhydria is present and causes a more severe anæmia than would result from the cancer toxins alone. At the same time neuro-toxins might well be produced.

Lastly, subacute combined degeneration of the cord is said to occur in connection with Addison's disease, although here again we have been unable to find any detailed reports. We have, however, had under observation a man suffering from typical Addison's disease with an extreme degree of pigmentation, a very low blood pressure, general asthenia and vomiting, in whom signs of posterior and lateral cord degeneration were present. Further investigation showed that the Addison's disease was associated with the blood changes of Addison's (pernicious) anæmia, so that the nervous changes can be regarded as a complication of the latter rather than of the suprarenal disease.

IX.—Subacute Combined Degeneration of the Cord without Anæmia.

It has generally been stated that cases of subacute combined degeneration of the cord occur without any anæmia. We have, however, seen no reports of such cases, in which blood examinations have been made during the last two or three weeks of life, and Byrom Bramwell's case, in which anæmia of a typical Addisonian form developed during the fortnight before death, shows how necessary it is to do this before concluding that the nervous disease runs its whole course without being complicated by anæmia. It would, however, not be surprising if in a small proportion of cases no anæmia occurred at all, because there is no reason why in some cases neuro-toxins might not be produced without hæmolysins, just as the latter are certainly produced in a considerable number of cases without the former.

X.—Pathogenesis.

In their classical account of subacute combined degeneration of the spinal cord published in 1900, Risien Russell, Batten and Collier [20] came to the conclusion that the disease is caused by some toxic agent, which is also the cause of the anæmia, with which it is generally

associated, and that it is not secondary to the anæmia. Writing ten years later, Buzzard [9] suggested that this toxin has its origin in the alimentary canal, and in 1921 Collier [11] concluded that the toxic agent responsible both for the nervous degeneration and the anæmia is of gastro-intestinal origin.

We have already given our reasons for believing that achlorhydria is an essential predisposing cause of Addison's anæmia. Our observations lead us to agree with Collier's most recent conclusion that the anæmia with which subacute combined degeneration of the cord is almost always associated is the so-called " pernicious " form, first described by Addison. It is therefore not surprising that achlorhydria appears to be present as constantly in cases in which subacute combined degeneration of the cord is the earlier and more prominent symptom, as in those in which anæmia is present alone or in which the nervous symptoms remain comparatively unimportant.

Gastric juice has two functions : it helps in the digestion of proteins, and the antiseptic action of its acid helps to protect the intestines from infection with swallowed organisms. In achlorhydria proteins pass into the duodenum in an unaltered form, and bacteria from the mouth and nasopharynx are likely to reach the intestine in far greater numbers than under normal conditions. If achlorhydria is associated with oral sepsis, secondary infection of the intestines is extremely likely to occur. The investigations of Bennett and Dodds [6] show that pancreatic secretion is also deficient in Addison's anæmia. The digestion of proteins is therefore likely to be even more deficient than in cases in which achlorhydria is present alone. Consequently in Addison's anæmia and in subacute combined degeneration of the cord intestinal infection is likely to be associated with the presence in the intestines of excess of undigested or incompletely digested protein. Under such conditions it is not surprising that toxins are produced by the bacterial destruction of proteins in abnormal quantities in the intestines. It is probable that one of these is specially toxic for the blood and leads to a hæmolytic form of anæmia, and that another is specially toxic for nervous tissues and leads to combined degeneration of the spinal cord. In most cases the former toxin is the dominant one, but in a small minority of cases the latter is the more important. Although one or other may appear to be present alone in the early stages, it is rare for the hæmolytic toxin and still more rare for the neurotoxin to continue to be produced without the other throughout the course of the illness.

XI.—Treatment.

The most important part of the treatment of subacute combined degeneration is to attempt to overcome the intestinal infection and so stop the development of the neurotoxic and hæmolytic poisons. Oral sepsis should be thoroughly dealt with. Every tooth which shows the slightest sign of infection on expert clinical examination should be condemned. An X-ray photograph should always be taken of all the remaining teeth, however healthy they may appear, and the slightest sign of apical infection or periodontitis should lead to their removal. In most cases every tooth will have to be extracted. If the tonsils are infected they should be enucleated, and the nose and nasal sinuses should also be examined and if necessary thoroughly treated.

The achlorhydria should be corrected by the administration of large doses of hydrochloric acid. In most cases we have found that a drachm and a half of dilute hydrochloric acid are required in order to compensate for the deficiency of gastric juice (Charts I and II). The acid should be added in the proportion of a drachm to 4 oz. of water in order to make a beverage, the acidity of which is about the same as that of gastric juice. If lemon juice and sugar are added the drink is quite palatable. It should be drunk during the course of each meal, and a little of it should be left over to sip for half an hour after the meal is completed. The patient should continue to take it without intermission for the rest of his life, as even if the intestinal infection appears to be overcome, the achlorhydria probably always remains.

Milk which has been soured with an active lactic acid bacillus should also be given for an indefinite period. Most patients can take half a pint three times a day without difficulty.

Lastly, a vaccine should be made from any streptococcus which can be isolated from the sockets of extracted teeth, from the duodenal contents withdrawn through an Einhorn tube, from the fæces and from the urine. This should be given in carefully graduated doses, beginning with very little, and slowly increasing, but it is desirable that no general reaction should follow the injections.

Unfortunately the degeneration of the spinal cord, when it has once occurred, is permanent, so that all that can be expected from adequate treatment of the intestinal infection is that the progress of the disease may be arrested. A certain amount of improvement may, however, result from a systematic course of exercises of the type that Frenkel introduced for tabetic ataxy. On the other hand, if the production of hæmolytic toxins is arrested, the blood shows spontaneous improve-

ment, and recovery can also be accelerated in severe cases by one or more transfusions of blood. Arsenic may be given, but care is necessary, as in the presence of subacute combined degeneration it is difficult to recognize the earliest symptoms of arsenical neuritis.

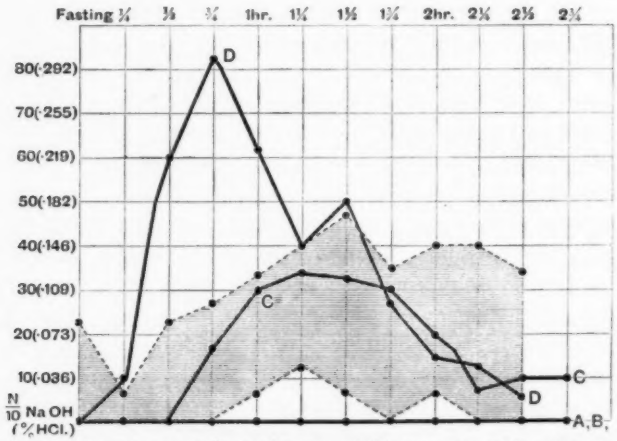

CHART I.—Fractional test meals to show free HCl in a man with subacute combined degeneration of the spinal cord. A, without addition of acid—complete achlorhydria; B, with addition of ʒi dilute HCl (B.P.) in ʒiv water (=0·3 % HCl) taken with the gruel and also sipped for an hour afterwards; C, with addition of ʒiss dilute HCl in ʒvi of water—normal curve; D, with addition of ʒii dilute HCl in ʒviii water—hyperchlorhydria curve. The shaded area represents the limits for free HCl of 80 % of normal people.

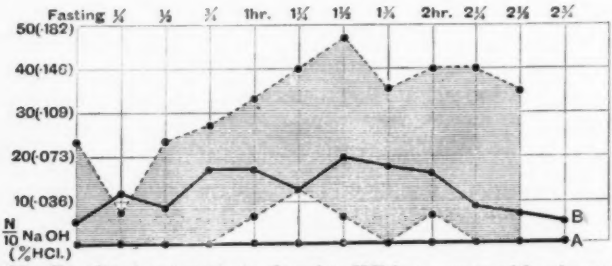

CHART II.—Fractional test-meals to show free HCl in a woman with subacute combined degeneration of the spinal cord. A, without addition of HCl—complete achlorhydria; B, with addition of ʒiss dilute HCl in ʒvi water.

Insufficient time has elapsed to be able to report the final result of treatment on these lines. So far it has been most promising. The anæmia, being recognized at an early stage, rapidly improves; in the two cases of our series which have been longest under observation it has

actually disappeared, and in one of these the red corpuscles now number over 5,000,000 per cubic millimetre. There has been no increase in the nervous symptoms or physical signs, and in one of the two cases just referred to the tingling of the feet and hands has almost disappeared, and the ataxic and spastic gait has greatly improved, but the physical signs are unaltered.

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THE MENINGIOMAS (DURAL ENDOTHELIOMAS): THEIR SOURCE, AND FAVOURED SEATS OF ORIGIN.[1]

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THE tumours under consideration have long masqueraded under so many guises that it is well-nigh impossible, historically, to do them justice. In their gross appearance, they are sufficiently striking to have attracted the notice of morbid anatomists from early times, and without carrying the subject farther back than Cruveilhier we may feel assured from the admirable illustrations in his famous "Anatomie Pathologique," that he at least had encountered before 1835 some four or five examples in the course of his extensive post-mortem studies.

As these, or similar tumours, were then known occasionally to involve and absorb the adjacent bone, a lively discussion had arisen as to whether they took their origin from the diploe or dura, and if from the dura whether from its internal or external surface. Earlier writers had referred to the lesion as a *fungus duræ matris*, a term which has survived to our times; but Cruveilhier substituted for this the designation *tumeurs cancéreuses des méninges*, thereby reflecting the pathology of his day, and as late as 1858 we find R. Bennett in this country using the term *epithelial cancer* for these meningeal tumours. Such epithets as these, however, could not survive the advent of the morbid anatomist armed with the microscope and aniline dyes, nor in turn the embryologist with his classification of tissues.

In the early days of histological pathology which had such an impetus in the 'fifties and which Sir James Paget in this country, the pupils of Johannes Müller in Germany, and Hermann Lebert, a disciple of Dupuytren, in Paris, had done so much to advance, it was customary to give descriptive designations to tumours. In 1854, in his celebrated lectures on surgical pathology, Paget confessed his inability satisfactorily to classify the large group of tumours "less malignant than cancer," to which Lebert had given the name *tumeurs fibro-plastiques*.

[1] The Cavendish Lecture, delivered before the West London Medico-Chirurgical Society, June 13, 1922.

He suggested the term *myeloid* or "marrow-like."[1] Billroth in 1856 gave the name *cylindroma* to a growth of the orbit which showed a peculiar tubular form of hyaline deposition, and at about the same time another term, still in common use for certain growths in which so-called "brain-sand" abounds, was first employed by Virchow. He had been among the first to call attention to the calcareous granules which, unrelated to any tumour growth, are found deposited in various situations in the cerebral appendages and meningeal envelopes. Though uncertain of their nature and origin, on finding these "sand-bodies" prevalent in two small dural tumours which had come to his attention, one arising from the olfactory groove and the other from the porus acusticus, he named them *psammoma*.[2]

Thus, names which are merely descriptive of degenerative processes of common occurrence in the tumours in question have since come to be widely employed.

At about this time there was a tendency among French writers, notably by Bouchard (1864), and by Robin [21], to substitute *epithelioma* for Lebert's "tumeur fibro-plastique," and when one considers that Robin was employing the current terminology for the lining of the serous spaces and vessels, and that he regarded the cells of the arachnoid as the source of origin of the growths, he deserves due credit for his views. This, however, was brushed aside by the greater authority of Rudolph Virchow.

In his classical "Vorlesungen" [23], though making some exceptions in regard to the psammomas, Virchow incorporated the tumours in question under the term *Sarkome der Dura mater*, and they continue for the most part to be so classified. However, in spite of their tendency to invade or absorb the bone, it came to be recognized that they were benign lesions of a peculiar histogenesis for which the designation sarcoma was inappropriate and misleading, and by the 'seventies this, in its turn, had begun to be qualified. Accordingly, such terms as

[1] In his celebrated "Anatomie Pathologique Générale," Paris, 1857 and 1861, Lebert describes and pictures as fibro-plastic tumours of the dura a few examples of these lesions, and in his "Surgical Pathology," Paget cites a most extraordinary example of a myeloid tumour which must have been a widespread bilateral and parasagittal meningioma with extensive hyperostosis cranei. The preparation is still in the Museum of St. Bartholomew's Hospital.

[2] Virchow came to regret the introduction (1859) of this term, because of its misuse by others. In a later article [24] he expressly states that an epithelial or endothelial tumour containing concrements is not a psammoma, that true psammomas have a connective tissue groundwork. This statement merely added to the existing confusion, though it is fair to say that psammoma bodies are apt to be more numerous in the older and more fibrous forms of meningeal tumours.

alveolar sarcoma came into use, and in France Cornil with Ranvier substituted *sarcome angiolitique* for Virchow's psammoma. But the term, sarcoma, however qualified, could not permanently survive the changing terminology of the embryologists.

Camillo Golgi, in an important article published in 1869 [14], called attention to the existing confusion in regard to these tumours. He had an opportunity to study two specimens, one of which was a typical tumour of the ethmoid region, which had come to light at autopsy in the hospital at Pavia, and he was the first to suggest the term *endothelioma* out of consideration for the employment by His of the word endothelium as opposed to epithelium. Thus, the simple term endothelioma was introduced in Italy, whence it has gradually made its way into other countries, but, unfortunately, even in the country of its birth, cumbersome word-combinations soon became attached to it. Bizzozero and Bozzolo [4], for example, soon subdivided the dural endotheliomas into three types, as *sarcoma endothelioides alveolare*, *sarcoma endothelioides fasciculatum*, and *fibroma endothelioides*, according to the manner in which the connective tissue elements behave in their relation to the endothelial cell nests, and whether endothelial or fibroblastic elements predominate. In this fashion, during the fifty years which have since passed, pathologists have vied with one another in modifying and extending the qualification "endothelial" to a wide range of tumours in a great variety of situations, in bone, thyroid, parotid, ovary, and elsewhere, into peritheliomas, hæmangio- and lymphangio-endotheliomas, and so on, with such hair-splitting refinements as to produce histological chaos.

In consequence of all this, the striking and characteristic intracranial growths we are considering, to which many of these names were first attached, have become so obscured by a multiplicity of designations that it is highly desirable to rescue and to re-assemble them under some simple caption. For this, Golgi's term, which has in later days gradually come to prevail, might suffice; but even this is now of questionable advantage, for it seems quite probable that, though attached to the dura, the tumours do not arise from this membrane proper, but rather from elements of the arachnoid which project into it; nor are they, in the parlance of some embryologists, tumours which, strictly speaking, actually originate from what are to be considered endothelial elements.

Not everyone has adopted Minot's "mesothelium" even for the cells lining the serous cavities, and it is quite evident that he had no

intention of including the meningeal spaces in this category, as some appear to have taken for granted. However, should the term be thus extended, and many anatomists so employ it, *arachnoideal mesotheliomas* would be the proper name for these tumours. But even if correct, this designation is too cumbersome for convenience, and it would seem best to sweep all these terms aside and adopt a label which is simple, and at the same time non-committal, except in so far as it indicates that the growths in question arise from the meninges. For this purpose the term *meningothelioma* was first proposed, but it has, on further consideration,[1] been shortened to *meningioma*. This word, consequently, will be used to indicate the entire group of tumours which appear to arise from the pachymeninx, whether mesothelial or fibrous elements predominate; whether the overlying bone shows hyperostosis or is unchanged; whether the growth is pedunculated or flat and widespread, and regardless of the degenerative changes and the presence or otherwise of psammoma granules.

These tumours, the meningiomas, have, as we shall see, favourite seats of origin and, though they may differ considerably in their histological picture, they are, as a rule, easily recognizable not only by their gross appearance but because of the fact that the stalk from which in their simpler form they seem to arise is so intimately incorporated with the dura that they appear to originate from it.[2]

[1] A note regarding the derivation of "thelium" and its combinations may not be amiss, and for the basis of what follows I am indebted to my colleague Frederick T. Lewis. The term *epithelis* (from ἐπί = upon; θῆλη = the nipple) appears to have been introduced by Ruysch early in the eighteenth century, and was first used for that transitional part of the epiderm at the lips and nipple—though in time "epithelium" came to be generally used not only for the two peripheral germ layers but for the lining of the serous and vascular spaces as well. In 1865 the word *endothelium* was first used by His as a designation for the lining membrane of these cavities arising from mesenchymal cells within the middle germ layer, and the term has come into general use not only for blood-vessels and lymphatics but all serous cavities as well. Kölliker in 1882 had used the term *mesepithelium* for the lining of the body cavities and urogenital epithelium, reserving the term endothelium for the vessels, synovial cavities, meninges, and so on; and to the same tissues Minot a few years later gave the name *mesothelium*. All three terms, *epi-*, *endo-*, and *mesothelium*, would appear to be unfortunate in view of their derivation in part from θῆλη, but they, nevertheless, have come to convey an idea.

[2] There are a few tumours which possibly are allied to the meningiomas, but which have no dural connection: they appear to arise from the pia. They are rare tumours of an angiomatous nature, whereas those under discussion are relatively non-vascular. Another still more rare tumour (particularly so in man) is the so-called cholesteatoma of the choroid plexus. It is actually an endothelioma with extensive psammoma deposit, and is often bilateral.

Incidence.

Some years ago all of the material relating to the several meningiomas, intraspinal as well as intracranial, then included in my tumour series, was gathered with the intent of publishing in detail our clinical and operative experiences with these interesting lesions. This project, however, was interrupted by the discovery that the acoustic tumours (neurinomas of Verocay), which in several instances had been diagnosed as fibro-endotheliomas, were distinctive tumours of an entirely different order. The "endotheliomas" were consequently dropped for the time being, in order to make a more thorough study of the tumours originating from the eighth cranial nerve, commonly described, in view of their location, as tumours of the cerebello-pontile angle.

In a monograph ultimately published on the subject of the acoustic tumours [8] it was pointed out that these lesions when bilateral are not infrequently accompanied by multiple small meningeal endotheliomas, so that tumours of these two types (neurinoma and meningioma) are in certain respects related. Nevertheless, it is far more usual for one or the other to occur in isolated form, and until something more is learned of a common ætiological factor it is undoubtedly best to consider them apart and as distinctive lesions.

The time has long since passed when we could hope to advance our knowledge of intracranial tumours to any great extent by considering them as a whole. Even their mechanical or pressure effects, which might be expected to be more or less similar in all cases because of the rigid character of the bony chamber within which they arise, differ widely, and it is notably true of these meningiomas that they may attain a huge size without giving rise to any of the so-called cardinal symptoms of tumour, notably headaches and objective changes in the eye-grounds.

Intracranial tumours, indeed, are so protean in form; they behave in such different ways; they provoke such varied clinical pictures; and the proper method of dealing with many of them, even when they are exposed by an operation, is in many cases still so problematical, that our only hope for progress is to particularize on certain groups of cases.

There are three ways in which a large material such as is before us may be profitably attacked. We may (1) concentrate our attention upon tumours of certain histogenetic types whatever their situation; (2) we may study tumours of all types in a given situation; or (3) what is perhaps better still, we may restrict our analysis, as was done with the acoustic tumours, to tumours of a single type in a given situation.

Only by the adoption of one of these methods can one's casual acquaintance with a disorder, made at the bedside or operating table, ripen into familiarity. Each has its advantages, but for the purposes of this particular study I shall adopt the first, and consider the meningiomas as a whole.

Verified Meningiomas.

On various occasions an explanation has been given of the system under which the tumour cases of my clinic are classified. They are listed as (1) *tumour verified*, when the character of the lesion has been histologically determined at operation or autopsy; as (2) *tumour unverified*, when the presence of a growth is reasonably certain or, indeed, when it may actually have been seen but without removal of a fragment for verification; and as (3) *tumour suspect* to include those cases referred to the clinic with a presumptive diagnosis of tumour, of the justification of which there remains considerable doubt.

In our present connection we are interested only in the 751 verified intracranial tumours, and without going into the detail, unnecessary for our present purposes, of distinguishing between the various sub-varieties of gliomas, adenomas, and so on, the cases may be tabulated as follows, in order to indicate the ratio of the meningiomas to other main tumour groups.

Table of Verified Intracranial Tumours to March 15, 1922.

Gliomas		314 cases	(41·8 per cent.)
Adenomas (chiefly pituitary)		159 ,,	(21·2 ,,)
Meningiomas		85 ,,	(11·3 ,,)
Neurinomas (acoustic)		63 ,,	(8·4 ,,)
Congenital tumours		40 ,,	(5·3 ,,)
(*a*) Suprasellar tumours (chiefly of pharyngeal pouch origin)	28		
(*b*) Cholesteatomas, dermoids, and teratomas	12		
Granulomas		33 cases	(4·4 per cent.)
(*a*) Gummas	12		
(*b*) Tubercles	21		
Papillomas (choroid plexus)		11 cases	(1·5 per cent.)
Angiomas		7 ,,	(0·9 ,,)
Metastatic and invasive		27 ,,	(3·6 ,,)
Miscellaneous and unclassified		12 ,,	(1·6 ,,)
		751	

The meningiomas, as can be seen, stand in about a one-to-four ratio to the gliomas or brain tumours proper, and if we add to this intracranial group of eighty-five cases twelve others which have arisen in

the spinal canal, there are, at the time of writing, nearly 100 tumours to deal with.

Anything like a complete analysis of these cases would far exceed the possibilities of a single address if the innumerable questions which would naturally arise were answered with any measure of completeness. The interest of the physician and neurologist would centre on the symptomatology and diagnosis--particularly upon the mistakes in diagnosis, and in these the psychiatrist, for reasons to be pointed out, is concerned perhaps more than any other. In the province of the ophthalmologist lie the visual field distortions, the examples of unilateral exophthalmos, and, above all, the changes—or what is possibly more important, the lack of changes—in the eye-grounds, for a choked disc may be absent or at least long delayed; on the other hand, in the supra-sellar lesions a primary optic atrophy may be the essential guide to the site of the lesion. Some of the tumours originate near the porus acusticus with loss of hearing as an early symptom, and so concern the otologist. Others which arise from the olfactory groove and invade the ethmoid cells come into the province of the rhinologist, and that newest of specialists, the endocrinologist, doubtless may have difficulty in distinguishing primary pituitary disease from the dyspituitarism secondary to one of these growths which so commonly arise from the meninges bridging the sella. And, last of all, the interests of the surgeon are focused on the methods employed for the removal, particularly of the more inacessible of these tumours, and upon the end results which may be obtained. Being one of them myself, the temptation is strong to yield to the desires of my own kind, and yet, in view of the very seriousness of his therapeutic measures, it behoves the surgeon, even more than others, to know all that he can learn regarding the origin, site, and characteristics of the lesion he plans to attack before he goes into action. I propose, therefore, though it is a somewhat less exciting story, to confine myself on this occasion largely to the two points mentioned in my title—the source, and the seats of predilection of the meningiomas.

The Source of the Tumours.

In 1911 an opportunity was afforded for an enlightening post-mortem study of one of these growths which had been undisturbed by previous operative manipulations. Including three spinal tumours, it was the fifteenth case in the series, and we were then still labouring under the impression that the growths took origin from the dura and were of

various kinds. Most of the preceding tumours had possessed a broad base of meningeal attachment, and until this case no particular attention had been paid to the meninges remote from the lesion, except to note the presence of multiple herniations which had early aroused our interest.

FIG. 1.—Fragment of calvarium overlying point of origin of tumour, showing slight invasion of inner table without hyperostosis. (Arrows show groove of sinus sagittalis.)

The patient, a woman aged 41, was admitted to the John Hopkins Hospital in a profound stupor, obviously in the terminal stage of compression from a brain tumour. An incomplete story was secured from a relative, of headaches for many years, of five months' confinement in bed with increasing disability of her left side, of progressive mental impairment, and finally of somnolence. She succumbed twenty-four hours after a first-stage osteoplastic procedure, at which time the dura was not opened. Had her condition at this first session justified a more prolonged exploration with exposure of the brain, the tumour would in all probability not have been disclosed, in view of its small surface area confined to the mesial edge of the hemisphere.

As is our custom at autopsy when circumstances permit, the brain was fixed before removal by a formalin perfusion through the carotids in order to preserve the pre-existing distortions which are otherwise considerably modified. On removal of the calvarium there was disclosed, about 5 cm. anterior to the Rolandic point, a small area (fig. 1) overlapping the groove of the

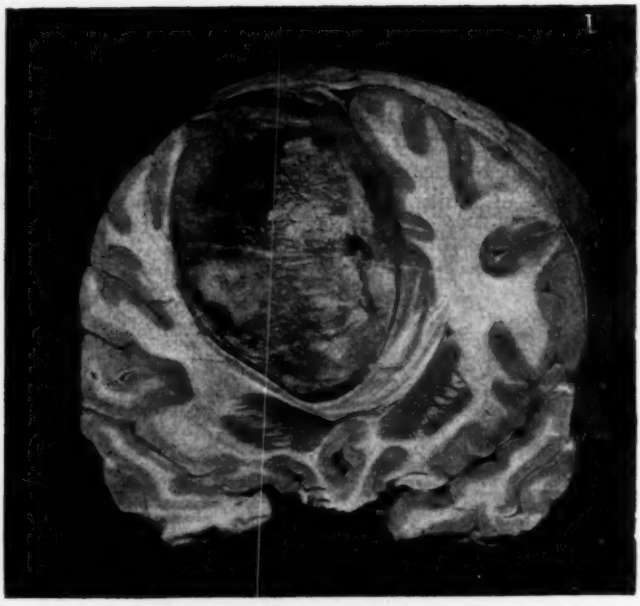

FIG. 2.—Coronal section through tumour, viewed from before, showing great dislocation of falx and corpus callosum.

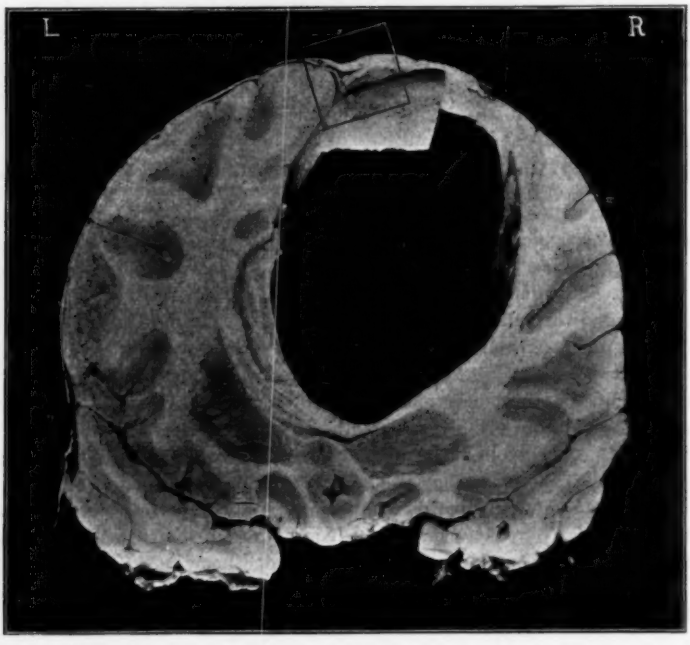

FIG. 3.—Coronal section viewed from behind, showing cavity occupied by the tumour and its only point of attachment under the lateral expansion of the sinus and at the angle of the falx.

sagittal sinus where the dura was adherent. The brain was removed, so far as possible, with its dural envelope intact, and a coronal section, through the point where the adhesions had been noted, transected a large tumour (fig. 2). of about 150 grm. weight, which had greatly deformed the hemisphere, and practically obliterated the ventricles. Except for the small stalk, from which the growth evidently arose, situated in the parasagittal angle and underlying the parasinoidal expansion of the sinus, the tumour was nowhere adherent (fig. 3). Hence, though apparently within, it actually lay outside of the hemisphere, whose pial covering remained intact over the deformed convolutions.

Microscopic sections through the point of meningeal attachment showed (fig. 4) that the tumour had invaded the sinus without thrombosing it, and though traces of the intervening dura still remained, it had been so effectually destroyed that to regard the sinus wall as the starting-point of the growth was an inevitable conclusion.

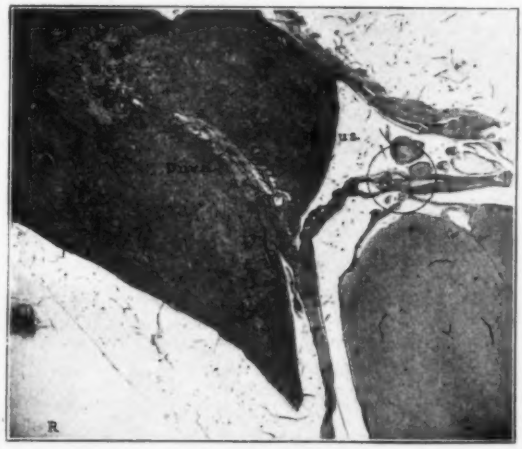

FIG. 4.—Section from area of attachment (squared area of fig. 3), showing invasion of sinus by tumour on right, and on left the arachnoid villi and cell clusters.

The lesion itself presented in different areas a most varied appearance. In some areas (fig. 5) it had a fibromyxomatous appearance, but for the most part (fig. 6) there were masses of endothelial cells with a more or less well-marked alveolar arrangement surrounded by bands of fibrous tissue, the cells of which in some places formed large fibrous whorls. Many areas showed extensive hyaline degeneration, and psammoma bodies together with so-called corpora amylacea were in abundance.

There is nothing unusual in the foregoing description of this particular tumour, for which a variety of names might be used. It

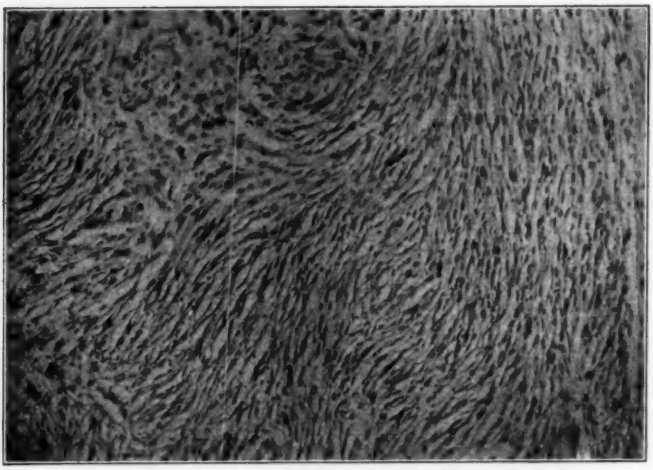

FIG. 5.—Fibromyxomatous area (mag. × 100).

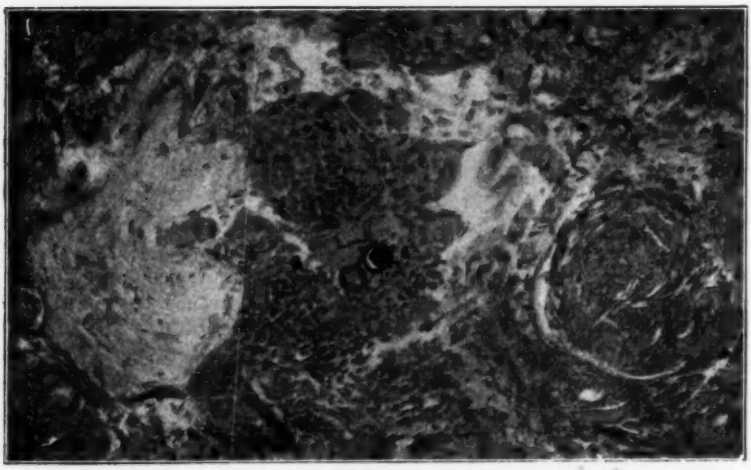

FIG. 6.—Endothelial cell alveolæ with fibrous whorls, psammoma bodies and hyaline areas (mag. × 100).

would probably deserve the term fibro-myxo-endothelio-sarcoma, and its seeming invasion of dura and bone would justify the assumption that it had malignant qualities which in time might have produced metastases. The whole story is essentially commonplace, and tumours of corresponding nature, beyond enumeration, have from time to time been reported in the literature.

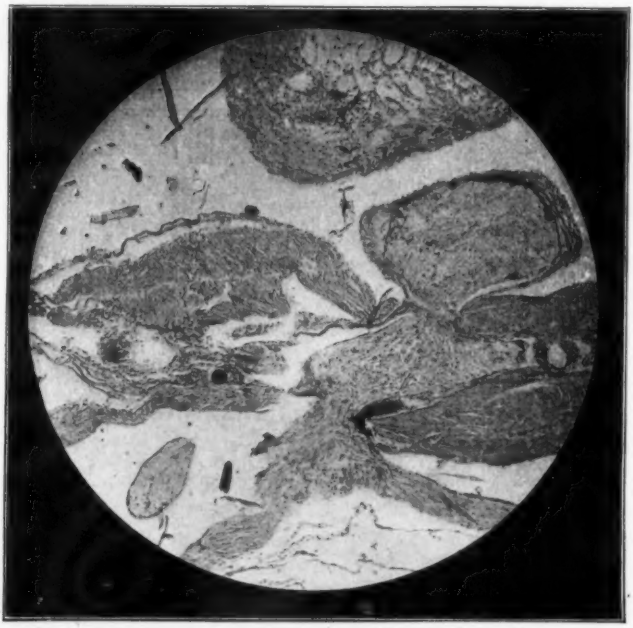

FIG. 7.—Showing an arachnoid villus projecting through dura into sinus. Also nests of arachnoid cells and psammona body lying within dura. (Area circled in fig. 4.)

But something apart from all this, of importance in our present connection, was observed in the meninges remote from the tumour. As already mentioned, the brain after fixation[1] had been removed with its

[1] A word in regard to this may not be amiss, for I believe that nothing has served to further our understanding of the mechanical effects of tumours so much as the abandonment of the time-honoured method of handling and sectioning the unhardened brain at autopsy after removing the calvarium and stripping off the dura. This unfortunate procedure, which is still an habitual one, has done much to delay our knowledge, particularly of the secondary disorders in cases of brain tumour which concern the cerebrospinal fluid pathway in ventricles, cysternæ and leptomeninges. For not only is the tumour topography largely altered if fluid escapes before the tissue has been fixed, but with the meninges stripped from the brain there has been little incentive in the past to study them in their relation to the adjacent cortex.

meninges largely intact, and sections through the unusually small stalk of the tumour gave a definite clue to the histogenesis of the lesion. Projecting into the sinus on the side of the uninvolved hemisphere were a number of hypertrophied arachnoid villi (fig. 7), capped by clusters of endothelial cells of precisely the same character and staining reactions as those of the alveolated masses of cells comprising the bulk of the tumour. Many of these cell-clusters disclosed in the dura showed a tendency to the familiar whorl formation (fig. 8), and in association with them were psammoma bodies in considerable numbers,

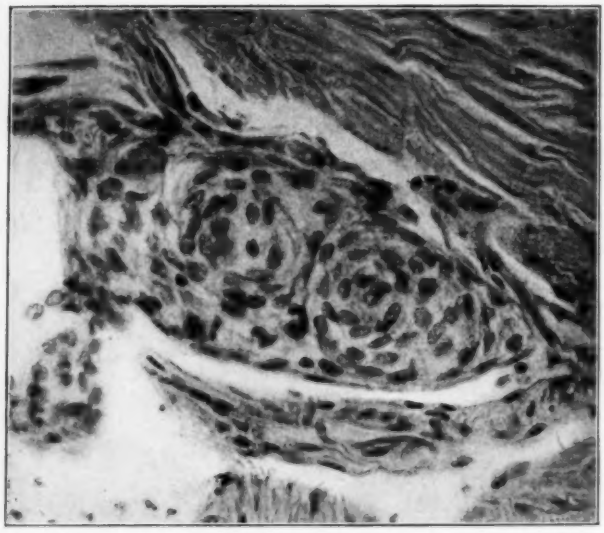

FIG. 8.—Showing typical cluster of arachnoid cells arranged in whorls and lying within dural layers remote from tumour.

In short, scattered through the uninvolved and presumably normal meninges were all the elements characterizing the tumour proper, these elements being of arachnoidal rather than of dural origin, though encased within the latter membrane.

This observation, so enlightening to us eleven years ago, proved, as will be seen, to be by no means an original one. It gave us, nevertheless, a new conception of the possible source of origin of these interesting tumours and suggested studies in two directions, the first of which might not have been so vigorously pursued had we then been

aware that our views were far from being novel. We undertook, on the one hand, a detailed study of the meninges in areas distant from the tumour in all similar meningeal growths; on the other hand, we began to investigate the arachnoid villi, and this in due course led us into a consideration of the cerebrospinal fluid circulation as a whole.

During the first two years after my transfer in 1912 to Boston, these studies, which had been started in the Hunterian Laboratory at the Johns Hopkins some time before, were continued in collaboration with Lewis H. Weed in the Laboratory of Surgical Research at Harvard, and due largely to his unusual gifts as an investigator considerable progress was made. In the series of papers which were published in 1914 [10], special attention was paid to the arachnoid villi whose function as points of escape for the fluid from the arachnoid spaces into the dural sinuses, though previously surmised, Weed, for the first time I believe, conclusively demonstrated.[1] The villi, in short, appeared to us to play a far more important physiological rôle than had been commonly ascribed to them. But before considering further this aspect of the subject and its bearings upon the tumour question, it is proper to make due acknowledgment to at least three authors by whom our views regarding the origin of these tumours proved to have been anticipated. It is not at all unlikely that there may have been others who have expressed similar ideas in papers under obscure titles which have not come to my attention.

In a brief article published in 1864, John Cleland [7], late Professor of Anatomy in Glasgow, set forth with prescience, the more remarkable when one considers the source of his material for study, the view that two tumours which he had found in the dissecting room, one of them arising from the cribriform plate and the other from the right frontal region adjacent to the superior longitudinal sinus, took their origin from the arachnoid rather than the dura. He observed that in structure they resembled the Pacchionian granulations in a number of points; that connective tissue bands ran through them, that concretions were present in both tumours, and new bone formation in one of them. In pointing out the proximity of these tumours to the falx, he mentioned the bony plaques often found attached to this membrane, and in agree-

[1] On his return to Baltimore, Weed's further pursuit of these investigations led, among other papers, to the publication of his monograph ("The Development of the Cerebrospinal Spaces in Pig and Man." Contributions to Embryology, No. 14. Carnegie Institution of Washington, Publication 225, 1917) on the development of the arachnoid, which represents the most important advance in our knowledge of the meninges since the classical work of Key and Retzius.

ment with Rokitansky attributed them also to the arachnoid rather than to the dura. Similarly, Ch. Robin [21] in France, described in 1869 two tumours likewise met with in the dissecting room. He also attributed them to the arachnoid, and in a long and scholarly article made a strong plea for their epithelial origin.

In another more extensive study published ten years before our interest in the matter was first awakened, Martin B. Schmidt, of Zürich [22], likewise called attention to the probable relation of the Pacchionian granulations to the so-called sarcomas and psammomas of the dura. In the course of his post-mortem examinations Schmidt had chanced to encounter twelve small meningeal tumours which he made the subject of special study. He was led to make a thorough histological survey of the meninges, and gave the first clear description of the microscopic islands of endothelial cells (Zellzapfen) which are found between the layers of the dura, in numbers which increase with advancing age in practically all individuals.[1] He recognized that these cell masses are related to the arachnoid tufts or villi, that they are themselves unquestionably of arachnoid origin, that they have certain seats of predilection, and, inasmuch as the cells comprising them were identical with those in the small tumours he had studied, he came to the same conclusion that Cleland and Robin, on less sufficient evidence, had reached years before, that they were the starting-point of these growths which, therefore, strictly speaking, have a leptomeningeal rather than pachymeningeal origin.

In medicine perhaps more than in other walks, discoveries are constantly being re-made and views being readvanced, for knowledge spreads slowly and facts once known and recorded are easily overlooked or forgotten. In 1915, in the last of our series of papers on the cerebrospinal fluid and its pathway, a paper chiefly devoted to the calcareous and osseous deposits associated with a cellular hyperplasia of the arachnoid [11], we in turn put forward as novel precisely the same views Cleland had advanced fifty years before regarding the derivation of these tumours from the arachnoid cell clusters. Five

[1] Others had observed these cell masses before Schmidt. They had possibly been seen long before by Rainey [20], who imagined them to be ganglionic structures which regulated the blood supply of the cerebral vessels. Fifteen years later Ludwig Meyer [18] [19] in a more accurate study of the meninges in cases of dementia referred to them as "epithelial granulations." Meyer recognized their relation to the arachnoid, noted the calcareous deposits which Virchow later named, and pointed out the relation of these cell clusters to the bodies of Pacchioni, which Luschka [16] a few years before had conclusively shown to be of arachnoid origin.

years later, Mallory [17] re-advanced the same views, and designated the tumours with the histological aspects of which he was chiefly concerned, as *arachnoid fibroblastomas*. Weed in the same year, though more interested in the physiological rôle of the membrane as a fluid container, nevertheless presented a convincing series of pictures from the meninges of the cat, showing that the clusters of cells may range from a moderate hypertrophy to actual tumours, in which most of the characteristic degenerative changes of these growths, as met with in man, occur.

Multiple Cerebral Herniations.

There is another matter relating to the arachnoid villi, apart from their histological characteristics and their possible relation to tumours, which had engaged the attention of a few pathologists. In 1870, before the Würtzburger Medical Society, von Recklinghausen exhibited as a curiosity a brain from a case of cerebral tumour in which small bits of cerebral substance, projecting into minute openings of the dura, more especially over the temporal lobe, had been torn off in the course of its removal. These minute lesions he recognized as multiple hernias of the cerebral substance. They had been observed by others long before him, by Cruveilhier for example, but no particular significance had been attached to them.

The matter excited no great interest until twenty years later when Benecke [2] reported as a great rarity two further cases showing these herniations, which he attributed to pressure. He pointed out that nests of endothelial cells were invariably present somewhere on the surface of the minute cerebral protrusions, and this led him to recognize their relation to the Pacchionian granulations.

Though in 1901 four other cases were incidentally recorded by Blasius [6] from Benecke's laboratory, the first thorough study of these lesions was published in 1908 by S. Burt Wolbach [28] who had observed them in a series of cases in which there had been tension, not, however, always due to tumour. Wolbach emphasized what is important in our present connection that the herniations occur in the regions where the normal arachnoid villi abound, a fact which carries with it the implication that the dural venous sinuses and their main branches are to be found in the same situations. He showed, furthermore, as did Schmidt, that these are microscopic or what one might call potential Pacchionian granulations, and concluded that "the multiple hernias of cerebrum and cerebellum always enter the dura through fissures occupied by arachnoid villi."

Though Schmidt himself published nothing further on the subject of the *Zellzapfen*, his interest evidently did not lag, for at least two papers, bearing on these matters, appear to have emanated from his laboratory. The first of them by Sophie Wojno [27] was on this subject of cerebral herniations which she recognized as occurring in the villi; but she dwelt chiefly on the fact that they may be found in conditions unrelated to tumour and attributed them, it would seem, to defects in the pia subjacent to the villi, which thereby permit the herniations to take place.

It may be recalled that all but one of the twelve meningiomas Schmidt had described were small growths and accidental post-mortem findings. Nevertheless, even under these conditions he had observed some of these herniations, more especially in the middle cerebral fossa. Apparently, therefore, he and his pupil were on the look-out for some explanation for them other than tension. They consequently were regarded as "physiological" herniations rather than pressure phenomena, and were attributed by Wojno to leptomeningeal defects.

There is, it seems to me, a much more plausible explanation of the presence of these herniations when there is no demonstrable increase of intracranial tension—a matter indeed very difficult to gauge by post-mortem appearances alone. In view of what we now know of the ease with which the brain takes up fluid and becomes œdematous, there are probably few individuals who with advancing years escape from periods of increased intracranial tension due to one cause or another. These must be particularly common in association with arterio-vascular disorders, and it is easily conceivable that the arachnoid villi under these circumstances may not only become hypertrophied into visible Pacchionian granulations, but that actual herniations may occur and subsequently recede with the subsidence of the œdema. Even in the presence of tumour when intracranial pressure is relieved by withdrawal of cerebrospinal fluid, by the intravenous administration of hypertonic salt solution, or more permanently by a generous decompression, it is not unlikely that these minute hernias may become reduced just as may the large hernias which protrude through operative defects in the skull. An illustration of this in the process of taking place is shown in the accompanying figure (fig. 9). The condition came to light during the study of the meninges of a patient who had been operated upon over the cerebrum through an error in diagnosis, when in reality there was a cerebellar tumour with internal hydrocephalus and great tension. A cerebrospinal leak communicating with

the ventricle occurred, and fatal meningitis was the result, but for the few days before death there was a complete release from the pre-existing supernormal tension; and at autopsy it was evident even to the naked eye that many of the large and multiple hernias which abounded were being withdrawn from their pockets in the arachnoid.

These minute herniations, as a matter of fact, are very commonly produced by long-continued states of increased pressure. That they project into and dilate pre-existing spaces there can be no doubt, and that these spaces communicate with the arachnoid is evident from the

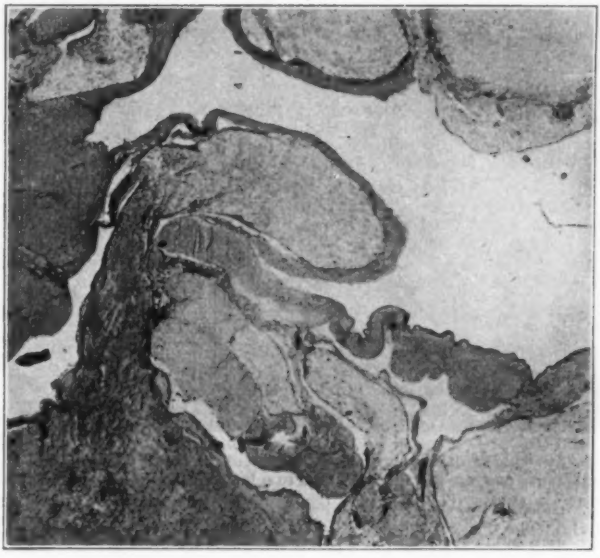

FIG. 9.—A cerebral hernia in the process of withdrawal from an arachnoid villus.

character of the cells lining them. What interests us chiefly at this time are the areas in which they are most commonly observed, since they betray the situations of the chief arachnoid villi and their associated cell-clusters. They abound, as might be surmised, along the major dural sinuses where the tentorium and falx unite with the dura over the cerebral and cerebellar convexities, but they are also to be found in the basal meninges, being especially common over the tips of the temporal lobes and in the region of the Gasserian ganglia, where they correspond likewise with the situation of the venous sinuses. They can be best studied in previously hardened brains removed with their

envelopes so far as possible intact; the accompanying figure (fig. 10), in which the relation of the protrusions to the branches of the vasa meningea media is apparent, gives an illustration of their distribution over the convexity.

FIG. 10.—Showing multiple herniations, projecting through the dura over the left hemisphere, produced by pressure due to a large suprasellar endothelioma.

ÆTIOLOGY.

Why should these cell-clusters in the arachnoid have a tendency in middle life to undergo tumefaction? An answer to this question, owing to the many and wide gaps in our knowledge, must be essentially speculative. However, some approach to it can be made. As in other tumours, the more obvious factors are age, congenital predisposition, trauma and physiological activity. Schmidt's original observation that the cell-clusters are absent or difficult to demonstrate in infancy and become more pronounced with increasing age, has been confirmed by others. In this connection the age of the ninety-seven patients with meningiomas, as recorded at the time of their admission to hospital, fall in the successive decades as follows:—

0—10	..	..	0	50—60	..	..	21
10—20	..	..	3	60—70	..	..	10
20—30	..	..	11	70—80	..	..	0
30—40	..	..	23	80—90	..	..	1
40—50	..	..	28				

These figures naturally represent the age when symptoms had become pronounced, and probably an average of five or ten years should be subtracted if one were to estimate the age of onset. Nevertheless it can be seen that these tumours, unlike the gliomas, are rare in the first two decades, and reach their maximum in the fifth, a decade at least later than the period of maximal frequency for the pituitary adenomas and the acoustic tumours.

The fact that in cases of neurofibromatosis (Recklinghausen's disease), multiple meningiomas occasionally co-exist with multiple neuromas of the cranial nerves, suggests that some congenital fault may be responsible. However, they occur singly with far greater frequency. Curiously enough, they bear unmistakably a close relation to trauma of one sort or another[1]. In so many of the cases in the series has a tumour been found at the exact situation where a stunning blow had been received on the skull years before, that this must represent something more than mere coincidence. On the circumstantial evidence it is tempting to assume that the injury has bruised the meninges and caused an extravasation, to aid in the absorption of which the local cell-clusters have been incited into a state of morbid activity. It is not improbable, too, as emphasized by Borst, that some form of injury other than a blow may serve to incite a pachymeningeal reaction and lead to tumour growth. In one of the cases included in the series, an unsuspected frontal endothelioma was found post mortem associated with a subjacent chronic abscess. Moreover, psammomas and endotheliomas have been observed by Berger [3], Dufour [12], Henschen [15], and probably by others, in connection with old cases of healed spinal tuberculosis in which there were unmistakable evidences of pachymeningitis. Henschen, in particular, lays great stress on this relationship in reporting a case which showed multiple tumours. They have been observed, too, in association with pachymeningitis interna hæmorrhagica. In explanation of all this it must be borne in mind that the cells which line the arachnoid actually represent an organ of great

[1] The youngest case in the series, for example, a boy of 13, with a 100-grm. meningioma which originated from the lower margin of the falx, had had symptoms for five years. He had received at birth an extensive cranial injury, associated in all probability with a tear of the falciform membrane.

functional potentialities. It is here that the studies of L. H. Weed and his co-workers have thrown a guiding light on the subject, for though an anatomist, Weed's interests have been on the side of function rather than structure.

To state the matter briefly, the arachnoid villi in close association with which the cell-clusters abound, act as organic filters interposed in the pathway of the cerebrospinal fluid, between the subarachnoid spaces and the dural sinuses. Their non-development or their occlusion by foreign particles, whether the product of injury or disease, or suspensions of substances such as lamp-black introduced artificially into the cerebrospinal fluid, will lead to stasis of the fluid and hydrocephalus, provided the occlusions are sufficiently widespread [26].

Furthermore, the cell-clusters under the stimulus of these injuries are prone to hypertrophic enlargement. It has been shown by Essick [13] that when the villi are experimentally blocked by particulate matter, whether sterile or the product of inflammatory reaction, the arachnoid cells proliferate abundantly, take on the function of phagocytes, and even become free-moving macrophages in the subarachnoid spaces. We may regard these cells, therefore, as agents which play a rôle in keeping the points of outlet of the fluid free from the mechanical obstructions produced by debris.

It is conceivable, therefore, that with advancing years the mesothelial cells comprising the cell-clusters are called upon from time to time to undergo periods of increased functional activity in their phagocytic rôle, after which they remain permanently hypertrophic or subsequently undergo the characteristic and well-known degenerative changes to which they seem predisposed. Hence their apparent increase in size and number with advancing age. On the other hand, some of the cell-clusters, possibly in consequence of these periods of activation, show neoplastic tendencies under certain circumstances obscurely related to the genesis of tumour formation in general.

The Situation of the Tumours.

It is evident from what has gone before, that at least four observers between 1864 and 1920 have independently come to the conclusion that these tumours, herein called meningiomas, are derived from the arachnoid cell-clusters. The relation of these groups of mesothelial cells to the functionating villi and of the villi to the dural venous sinuses, has been emphasized. It has been shown further that the

places where the villi abound is indicated by the distribution of the minute cerebral hernias which protrude into them in cases of marked intracranial tension. It remains to be seen whether there is any definite correspondence between these regions and the points of origin of the tumours themselves.

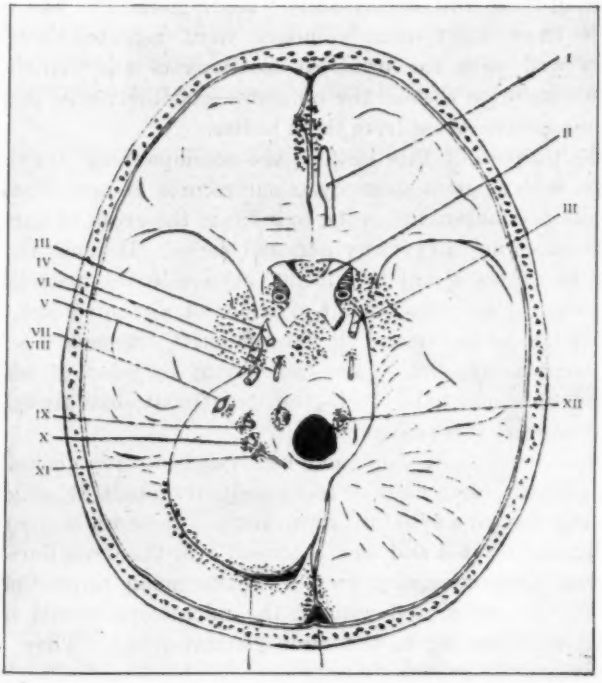

FIG. 11.—From Aoyagi and Kyuno, showing the situations of the cell clusters.

The only paper on this subject, to my knowledge, was published in 1912 by Aoyagi and Kyuno [1] and for a translation from the Japanese I am indebted to Professor Tanaka, of Okayama. These authors made studies of the dura of individuals of various ages to determine the seats of predilection of the arachnoid cell-clusters, and identified their presence in the following situations (fig. 11), viz., along the sinus sagittalis superior; near the crista galli; the sinus transversus; surrounding N. oculomotorius, trochlearis, abducens, and trigeminus; around the hypophysis; near the sella turcica; the plexus basilaris; at

the point of penetration of the dura by the third, seventh, ninth, tenth, eleventh and twelfth cerebral nerves; and also at the points of penetration of the nerve-roots of the cervical spine.

Furthermore, they gathered from the literature thirty-six cases of so-called dural tumour (variously termed sarcoma, psammoma, endothelioma, sarcomatous endothelioma, spindle-cell sarcoma, &c.) and added three cases of their own, all evidently "meningiomas." The situations in which these thirty-nine tumours were reported corresponded sufficiently well with the principal locations of the cell-clusters to justify the conclusion that all the tumours—endotheliomas, psammomas and sarcomas alike—arose from these bodies.

For the purpose of this lecture, the accompanying drawings have been made, with as great accuracy as our records of operations and the study of autopsy material permits, to indicate the areas of dural attachment of the meningiomas in my personal series. It must be admitted that in certain cases it may be difficult, even with the material in one's hand, to judge of the exact point of origin of a meningioma. This is particularly true of the spreading flat tumours[1], for such a small stalk of attachment as appears in the case herein recorded in some detail (figs. 2 and 3) is unusual even in the large potato-like growths which tend to be more or less pedunculated.

The meningiomas, in short, may be divided into two general classes: the large growths, often more or less irregularly lobulated, which incline on the whole toward a spherical form, and the tumours *en plaque* which are but slightly elevated and tend to spread over the inner dural surface. These latter meningiomas represent but a small proportion of the tumours in the series, and without the microscope would hardly be recognized as belonging to the same general group. They are more common among the growths arising from the basal meninges than from the convexity, though three of them occupied the parasagittal angle and a number have been found spreading over the dura in the sphenotemporal region. In this latter situation they appear to arise from near the pterion, where the meningeal vessels and sinuses so commonly channel the bone. Though these meningiomas *en plaque* are but slightly elevated and resemble a granulomatous meningitis rather than a new growth, they are particularly prone to push through the dura and to invade the overlying bone.

This tendency of the meningiomas to provoke a cranial hyperostosis

[1] An example of one of these lesions, which are particularly apt to be associated with an overlying hyperostosis cranei, has been recently reported in another connection [9].

constitutes a story by itself, and it must suffice to say that a considerable percentage of all these tumours produce a marked effect on the adjacent bone. There may be a very slight involvement of the inner table (as in fig. 1), or a marked endostosis corresponding approximately to the centre of the area of dural attachment which is indented thereby. Occasionally the bone is enormously thickened over the growth, as much as three or four centimetres in extreme cases, and under these circumstances the canaliculi are filled more or less extensively by tumour cells, which in time may replace the thickened bone by a core of solid tumour. These characteristics are schematically shown in the accompanying

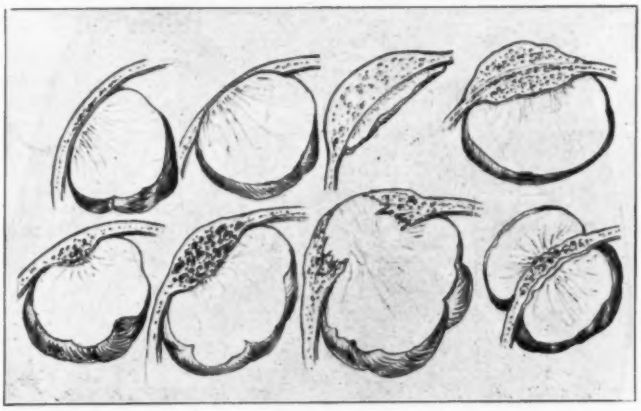

FIG. 12.—Diagrams of the various ways in which the meningiomas affect the overlying bone.

drawings (fig. 12), and they are mentioned because the photographs, X-rays and measurements giving the situation of these hyperostoses have been an additional help in placing the situation of a number of the tumours in the series. There are other ways by which the location of the seat of origin may be identified with fair accuracy, though chief reliance has been placed on the sketches and diagrams of the operations which accompany the old case records.

With due allowances, the plotted charts (figs 13 to 16) are sufficiently dependable. Though self-explanatory, there are certain features to which attention may be called. It is evident that the lesions are more numerous in the frontal regions, both of the vault and base, so that the frontal lobes have been involved through deformation far more often than any other part of the brain. Many years ago attention was

called by Blackburn [5] to the fact that frontal endotheliomas are a not infrequent post-mortem finding in those who have died in asylums, but until these diagrams were made I would not have believed that the tumours in our surgical series would, on the whole, have tended to be so far forward.

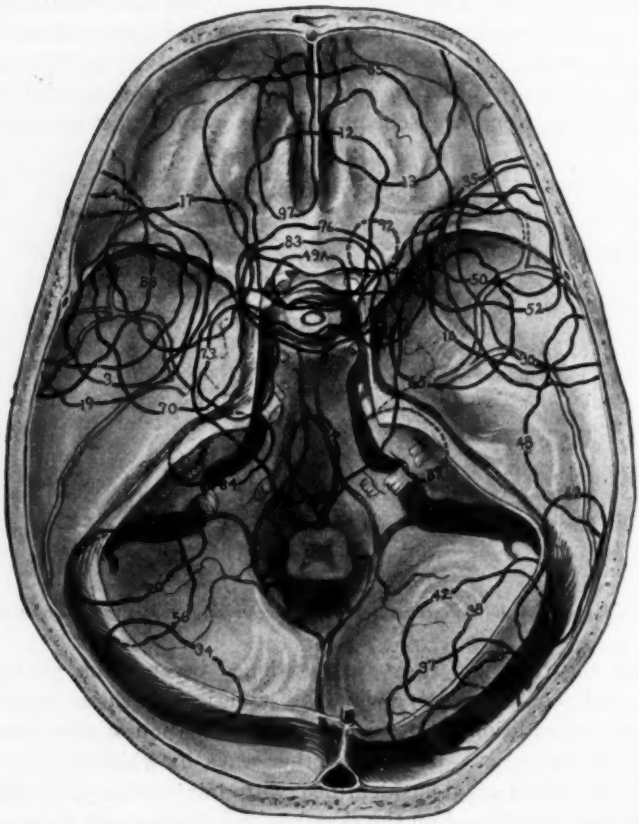

FIG. 13.—To show the areas of dural attachment of the meningiomas in the series in their relation to the major sinuses of the basal meninges.

Unquestionably many of these lesions are never recognized during life, and even if a diagnosis of "tumour suspect" actually be made, the localization of the lesion may be extremely difficult in the absence of an area of hyperostosis, either palpable or shown by X-rays. It is possible, therefore, that the blank areas in the diagrams merely repre-

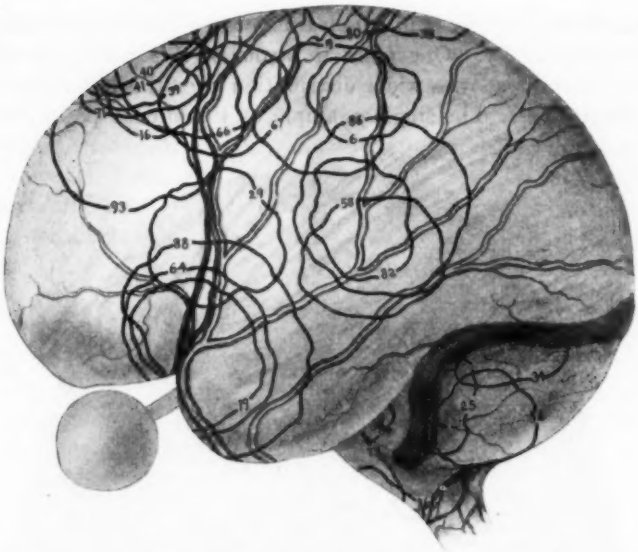

FIG. 14.—To show areas of dural attachment of the meningiomas and their relation to the dural sinuses on the left lateral aspect of the brain.

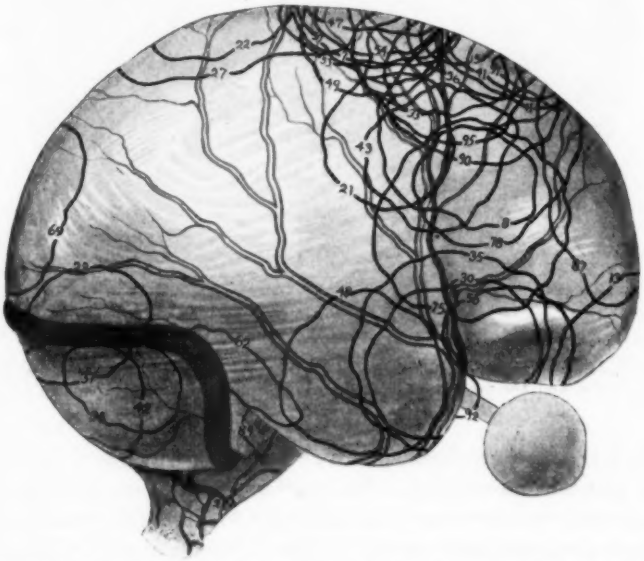

FIG. 15.—To show areas of dural attachment of the meningiomas and their relation to the dural sinuses of the right lateral aspect of the brain.

sent relatively silent fields in which tumours are less likely to have been recognized clinically. One point in favour of this is the fact that the recorded tumours show a wider distribution over the left than over the right hemisphere. The single example of tumour far posterior on the

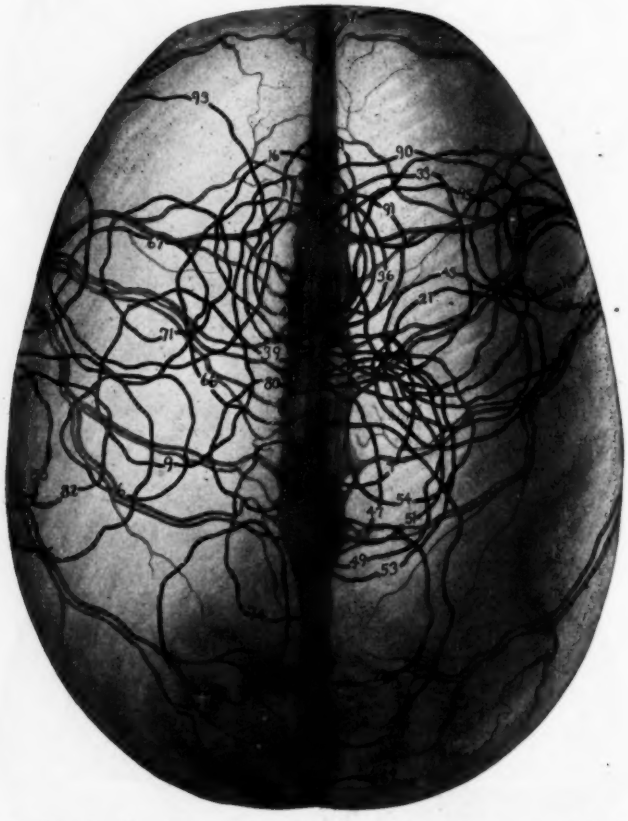

FIG. 16.—Superior view of the meninges, showing the tendency to an anterior disposition of the tumours, and the prevalence of their origin from the lateral expansion of the sinus sagittalis.

convexity of the right hemisphere (No. 27, fig. 19) was a purely accidental post-mortem finding. The patient was an acromegalic with a primary optic atrophy and homonymous hemianopsia attributed to a pituitary adenoma, and owing to the combination of his profound psychosis and an inaccurate clinical history he passed through our

hands with the meningioma unsuspected. He died a year later in an asylum, where at autopsy a large parasagittal meningioma (fig. 17) was unexpectedly disclosed.

Mere diagnostic oversight, however, cannot alone explain the predominance of anterior lesions, for notably in the posterior fossa under the tentorium, where localization should be easy, meningiomas are particularly rare. This is true, also, of the growths involving the occipital lobe, of which there have been only three in the series,

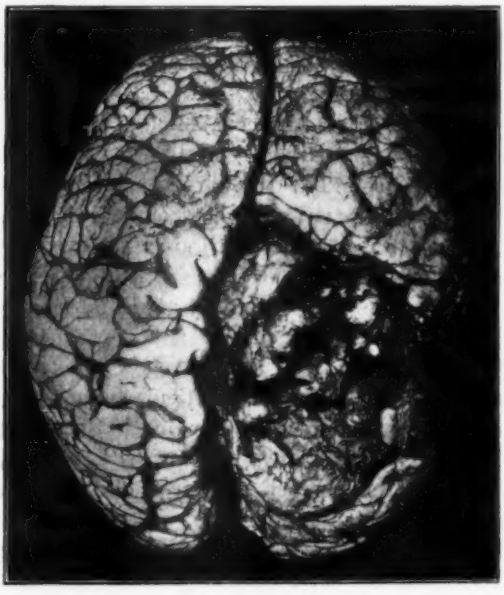

FIG. 17.

whereas on the other hand the extraordinary prevalence of tumours which take their origin from the meninges of the suprasellar region and cribriform plates of the ethmoid cannot be accounted for on the basis of chance alone.

I have spoken of the three ways of approaching the study of a large series of tumours and, so far, have refrained from any discussion of the meningiomas according to their locality. The endeavour has been made with no great success to subdivide them for working purposes into several clinical groups. These may deserve a brief mention.

(1) *The spinal meningiomas.*—These occur at different levels of the cord, and judging from my small series of twelve cases in which the greater number are midthoracic, they arise more often from upper than lower areas of the spinal theca. They are well-known lesions, frequently operated upon with success since 1888, when Horsley and Gowers so brilliantly led the way. What, however, is not commonly recognized, or at least emphasized, is the fact that they take their origin from the arachnoid at the point of emergence of one of the nerve-roots, so that the growth usually lies at the side of the cord, and is overlain by the nerve-root in question. This explains the characteristic discomforts of these cases, and the frequent tendency to a Brown-Séquard type of spinal palsy.

(2) *The cranial-nerve foraminal tumours.*—These cases fall into three groups, though they may be capable of greater subdivision since the cell-clusters from which they arise are said to exist at the foramina of exit of all the nerves. The tumours we have encountered have arisen (*a*) at the porus acusticus with loss of hearing as the inaugural symptom, suggesting an acoustic neurinoma (1 case); (*b*) from the trigeminal sheath, a common seat of origin, with trigeminal pain and hypæsthesia as early symptoms (5 cases); and (*c*) in the orbit itself, from the arachnoid sheath of the optic nerve, producing a unilateral painless exophthalmos (1 case).

A peculiarity of the basilar tumours, particularly those of the trigeminal region, is that they may spread widely in the basal meninges and become thereby irremovable. This, however, is not invariable, for one tumour (No 26) in the series which arose from the dura over the basilar process just within the foramen magnum, was egg-shaped with a small stalk of attachment.

(3) *The suprasellar tumours.*—These are fairly common, the series containing eight examples. The tumours arise from the meninges covering the Willisian circle of sinuses surrounding the pituitary diaphragm. Except for the fact that they occur in adults, whereas the suprasellar tumours originating from the cranio-pharyngeal pouch (Rathke) usually give symptoms in childhood, the manifestations of the tumours of the two types are very similar, consisting chiefly of primary optic atrophy, of field distortions often with hemianopsia, and finally of secondary dyspituitarism.

The growths may project upward into the region of the third ventricle, and may reach an enormous size. As several of them have been unexpectedly encountered at operations conducted for presumed pituitary tumours, they have merely been verified by the removal of a

small fragment of tissue and, except in one instance where a small, easily dislodged tumour was found, no attempt has been made to extirpate them. Consequently, except for the two cases encountered at autopsy, both of which show a remarkable similarity, the exact delimitations of the areas of attachment are somewhat conjectural.[1]

(4) *Tumours arising from the olfactory groove of the ethmoid.*—In Cruveilhier's plate one of these characteristic growths is pictured, and the later literature contains reports of many others in the same situation. Though more anterior than those just referred to as suprasellar, the growths have very much the same appearance. They are exceedingly difficult to diagnose. Occasionally a fortunate stereoscopic X-ray may show some local bone absorption and unexpectedly reveal the situation of the lesion, but otherwise there may be nothing more than some obscure mental derangement possibly with anosmia until the growth extending backward reaches a sufficient size to press upon one or both optic nerves. The tumour may be median and separate the two frontal lobes widely, or, if unilateral as in the single case in the series in which a total extirpation was successfully accomplished, it may press upon the homolateral optic nerve and give a primary atrophy, whereas the opposite eye shows a choked disc.

(5) *Sphenoidal ridge tumours.*—The growths which lie astride the sphenoidal ridge, with a portion of the tumour resting on the orbital plate under the frontal lobe and a portion in the middle fossa indenting the temporal lobe, are fairly common and characteristic. Most of them have been unexpected findings, though one or two have been recognized because of an absorption of the sphenoidal ridge shown by an antero-posterior röntgenogram. They may cause uncinate seizures and not infrequently encroach on the side of the chiasma and produce an homonymous hemianopsia.

(6) *Sylvian cleft tumours* (*temporo-frontal*).—These are, on the whole, similar to the above and doubtless arises from the same sinus, but they lie sufficiently far lateralwards to be brought into view by a subtemporal decompression. Two of them which gave no localizing symptoms were unexpectedly disclosed in this way and were subsequently removed by an osteoplastic exposure. In this region, too, for some unexplained reason, the tumours *en plaque* are common, and as these meningiomas are apt to provoke hyperostosis and cause a palpable thickening of bone at the temporo-sphenoidal junction, they are easily

[1] One of these cases was fully recorded because of its pituitary manifestations in my monograph, "The Pituitary Body and its Disorders," 1912, Case No. viii, pp. 63-72.

recognized through this indication of their presence, as well as by the marked exophthalmos which occurs if the hyperostosis involves the outer orbital wall.

(7) *Tumours of the convexities.*—These, twenty-eight in number, naturally represent a large proportion of any surgical series. They are not only easily accessible, but when they encroach on the sensori-motor cortex, characteristic and well-known symptoms of definitely localizing value are often produced. For this reason, small surface meningiomas which cause Jacksonian seizures followed in time by palsy not uncommonly fall to the lot of the general surgeon.

The tumours arise from arachnoid cell-clusters in connection with the spheno-parietal sinus and the vasa meningea media. They may be subdivided into *temporal, frontal, paracentral, parietal* and *occipital* tumours, and the diagrams show that in spreading up from the last described group which centres around the Sylvian notch, they dispose themselves in some correspondence with the fan-shaped distribution of the sinusoidal veins of the dura. They predominate over the frontal areas and their points of origin may be found even as far forward as the tip of the lobe. The series contains no examples of tumours arising over the posterior surfaces of the hemispheres except those which take origin from the major sinuses. They are included in the following groups:—

(8) *The parasagittal meningiomas.*—These, in a way, are the most interesting and characteristic of all. The case (No. 15) selected as a text for this lecture was of this type, and the series contains twenty-six other examples. The tumours arise from the wall of the sinus or its lateral expansion, and are apt to have some attachment to the surface of the falx as well. Consequently, as the growth enlarges, the mesial edge of the hemisphere gets pushed away to a greater or less extent from the parasagittal angle.

When a parasagittal tumour is surmounted by a dome of hyperostosis, its situation and identity are easily recognized. Also when Jacksonian seizures originating in a foot are followed in the course of years by a spastic paralysis which begins in the corresponding leg, one may feel reasonably assured that a parasagittal meningioma will be disclosed at operation, provided the mesial edge of the hemisphere can be brought into view.

When, on the other hand, the parasagittal tumours arise well in front of the motor cortex or, what is less common, posterior to it, they may be exceedingly difficult to localize by symptoms alone. An example

of this has already been cited in connection with Case 27 (fig. 17). There have been only two tumours in the series deforming exclusively the occipital lobe. One of them (No. 69, figs. 15-16), a parasagittal tumour originating near the tentorial angle, was successfully enucleated with perfect recovery. The other, a huge 200-grm. tumour not represented in the diagram as its point of origin remains obscure, was incompletely removed, and there was a continuance of the growth with fatality at a secondary operation some years later.

(9) *The meningiomas of the falx.*—No mid-line diagrams permitting the representation of these tumours have been made, for the series contains only two examples. Both of them were large tumours of almost spherical form, with the smallest possible area of attachment at the lower margin of the falx. Their presence in each case was identified by exploratory punctures, and both were removed by transcortical incisions with death in one case and recovery in the other.

This I cannot believe represents fully the true percentage of tumours originating from the sides of the falx, for bony plaques and endotheliomatous patches, as is well known, are not uncommonly found there in the ordinary run of post-mortem examinations on old people.

(10) *Tumours of the sinus transversus and sigmoideus.*—The series contains only two supra-tentorial tumours of this origin (Nos. 62 and 23, fig. 15). One which gave no localizing symptoms was first unexpectedly exposed during a right subtemporal decompressive operation. Its comparatively small attachment corresponded to the knee of the sigmoid sinus. One other (No. 23) was farther posterior, a large tumour which had caused a hemianopsia.

On the other hand, there have been five subtentorial tumours giving a cerebellar syndrome. All of them arose from the lower wall of the transverse sinus, and all were successfully removed at operation. I confess to some surprise that these growths are not more common in this situation, in view of the abundance of arachnoid villi which project into the subtentorial wall of this sinus and which all surgeons familiar with cerebellar explorations have been accustomed to observe.

These, then, are the chief topographical subdivisions into which the tumours have been tentatively grouped for clinical purposes. Doubtless some far better regional classification will be made as the particular symptom-complex called forth by a growth in these several regions comes to be more clearly understood. Certain of them, like the parasagittal tumours which impinge on the motor cortex, can with a fair

degree of diagnostic accuracy be foretold before operation, but in the absence of an accompanying hyperostosis most of the others are as yet chance findings in the course of an exploration, though a long history of slowly advancing trouble may make one suspect the presence of a meningioma.

I hope some day, using this lecture as a basis, to give the detailed report of the individual cases in this series with their triumphs as well as their tragedies. Our experience may be summarized as follows: (1) A few of these tumours have been accidental post-mortem findings in patients in whom brain tumour was unsuspected; (2) three of them have been late post-mortem findings in patients who had been operated upon some years before for presumed tumour, but as this procedure revealed neither tumour nor tension the cases had been variously diagnosed as some condition other than tumour; (3) in some of the cases (possibly ten) the growth, which produced no localizing symptoms, was accidentally disclosed during the course of a subtemporal decompression; (4) in the majority of the cases the presence of a tumour was obvious and its location definite, but there is no pre-operative statement in the case history to show that its nature was anticipated; (5) in a few of the operated cases not only was the location of the tumour evident, but a presumptive diagnosis was made of its character. This, of course, applies to all tumours with hyperostosis, as well as to several trigeminal, suprasellar and parasagittal lesions without osseous changes. Naturally, if one makes a diagnosis of meningioma in all patients with symptoms of brain tumour, he will be correct in about 10 per cent. of his cases, but we should aspire to something far better than this low figure.

The foregoing rough subdivision is made in order to encourage others and to spur ourselves in an effort to enlarge the percentage of cases falling in the last group. Certainly, with our present knowledge of these lesions we should to-day with a corresponding group of cases be able to make a correct pre-operative diagnosis in at least half of them. Small tumours such as those described by Schmidt as accidental post-mortem findings give no recognizable symptoms and have no surgical bearing unless they happen to impinge upon some important cortical area and provoke Jacksonian seizures. But the larger tumours, even when in silent areas, ought to be capable of recognition if chronology and duration of symptoms, age of patient, extracranial circulatory signs and the frequent hyperostoses are taken into account. Accordingly, it should be possible in an ever increasing percentage of cases to foretell

not only the situation of the growth, but to anticipate its character as well. This, in an operation so elaborate as one for brain tumour, is an enormous advantage.

There is no gainsaying that despite the enucleability of these tumours when they are easily accessible the operations are often attended with great hazard, and more often than in the case of other tumours this must be done in two or even three sessions. One reason for this is that before its presence has been even suspected, the growth may have attained a large size, and by venous stasis have greatly increased the vascularity of scalp and bone.

There is to-day nothing in the whole realm of surgery more gratifying than the successful removal of a meningioma with subsequent perfect functional recovery, especially should a correct pathological diagnosis have been previously made. The difficulties are admittedly great, sometimes insurmountable, and though the disappointments still are many, another generation of neurological surgeons will unquestionably see them largely overcome.

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Notices of Recent Publications.

The Mechanism of the Brain and the Function of the Frontal Lobes. By Professor Leonardo Bianchi. Authorized translation from the Italian by James H. Macdonald. Pp. 384. Edinburgh: E. and S. Livingstone. 1922. Price 21s. net.

Professor's Bianchi's views on the functions of the frontal lobe are based on numerous experiments on the brains of animals, chiefly monkeys, carried out over a long period of time. Interpreting the results of these experiments in the light of his study of the evolution and structure of the frontal lobes and of the pathways connecting them with the rest of the brain, as well as the various doctrines of neuro-physiology to which that study gives rise, Bianchi is convinced that in man these lobes are specially concerned in the synthesis and elaboration of the higher intellectual and sentimental processes, and all the various attributes of sociality. They play a most important part, he holds, in the formation of the psychic personality, and the development of the powers of conscious volitional behaviour.

Professor Bianchi divides the cerebral cortex into two main evolutionary levels, the postfrontal motor and sensory areas, and a prefrontal area that is neither motor nor sensory; he also postulates two grades of psychic activity, a "lower" and a "higher" consciousness, resulting from the activity of these two levels. In the lower or postfrontal consciousness, only the simplest mental constructions obtain; life is centred around sensations, desires, and instincts; conduct is impulsive and egoistic, and tends to the immediate satisfaction of individual needs only. In the higher or prefrontal consciousness, reason and all the potentialities of thought come into play; and impulses become subject to voluntary inhibition and control and are influenced by factors arising from the development of the more lofty sentiments and the higher social tendencies and obligations. When Bianchi speaks of the higher consciousness as prefrontal he does so only in the sense that it is the prefrontal area of the cortex that contributes to it its most weighty factors. Its centre of centres is in the prefrontal area, but it is necessarily open, he maintains, to currents from all parts of the cerebral mantle, and it thus comes to form with the lower consciousness a wide network of ideas and experiences which embrace the products of all the cortical centres. That power of starting, directing, evoking and selecting the nervous currents, possessed in a minor degree by all the cell-groups of the cortex, belongs in supreme part to the prefrontal area. In Bianchi's view, therefore, the frontal lobes are the seat of the final synthesis and fusion

of the incoming and outgoing products of the several sensory and motor areas of the brain.

The work of the brain, as a whole, is carried on by processes occurring in different levels of physiological complexity, the later and more highly evolved areas assimilating, synthesizing, and modifying the products of other lower subsidiary levels, and in dealing with the highly complex psychical end-products of prefrontal synthesis. Bianchi sees no reason for treating them differently from the other products of cerebral activity of a more physical character, or thinking that their governance is by laws in any essential way different from those that obtain in the more purely physiological sphere. He discusses the results of frontal lobe activity, therefore, wholly as biological products, not as spiritualistic or metaphysical abstractions, and in doing so necessarily lays the greatest stress on the multitudinous combinations of innumerable lesser grade compounds in their final elaboration. What it involved in the last analysis, in the psychic transmutation or "mentalization" of matter, may be still open to conjecture, but even here Bianchi offers some suggestive speculations in regard to the light which the study of the behaviour of electrons may throw on the subject.

Professor Bianchi's opinions concerning the function and relationship of the different parts of the brain, founded as they are on the results of extensive experimental investigations, must command our respect, while his careful attempt to evaluate psychic phenomena on a biological basis affords us no slight glimpse into the mechanism of the brain's activity, and serves as a stimulating corrective to those aspects of psychological thought which tend to divorce mental processes from their physical substratum. His insistence too, at the end of his book, on the primary importance of rightly trained, conscious intention and intelligence in the conduct of the practical affairs of life is especially valuable at a time when, too often, the "urge" of the unconscious is apt to be used as an excuse for the lack of that self-control and sense of responsibility, for the cultivation of which he pleads. He expresses "grave doubts" indeed, of the automatism of the unconscious, apart from any directive effect due to the action of the conscious will.

A word in conclusion must be said about the translation of this book. Dr. Macdonald has done this in a way that cannot be too highly praised, and has given us a scholarly English version, in all respects worthy of its distinguished author.

Questions neurologiques d'actualité. Pp. 551. Paris: Masson et Cie. 1922. Price 28 francs.

In this volume there are collected together twenty lectures on neurological subjects of special interest delivered before the Faculté de Médecine de Paris in 1921. Each of the lecturers was free to choose the subject that appeared to him of most importance at the moment, and each subject selected has been consequently dealt with by one capable of placing before his audience views of an authoritative and reliable nature.

In most cases the aim of the lecturer has evidently been to put forward the observations and opinions on his subject that appeared at the moment most trustworthy rather than his own personal views, but many of the articles show evidence of original investigation and research. In some instances, however, the lectures are based on the original investigations of the authors; this is particularly so in Kinnier Wilson's contribution on the pathogenesis and pathological physiology of progressive lenticular degeneration, and in Pierre Marie's discussion of the question whether preformed and innate centres for speech exist in man. In both of these, as well as in Claude's paper on intracranial hypertension and serous meningitis and in Lhermitte's on lethargic encephalitis, in which the subject matter consists mainly of original work already published, we are fortunately provided with the views these neurologists hold to-day after reviewing their earlier work in the light of further experience and criticism. A few of the lectures on the other hand merely represent the ordinary teaching of the day, without any analysis or critical selection of facts and hypotheses.

There are, however, few of these lectures which will not repay perusal by any neurologist, and all will be valuable to the general physician and even to those specialists who are unable to keep pace with the neurological literature.

The only serious fault that can be found with the volume is absence in almost all the articles of bibliographic references to the work of others which is cited.

Report of the War Office Committee of Enquiry into "Shell Shock." H.M. Stationery Office. 1922. Price 6s.

The reference to the Committee was to collate the expert knowledge derived by the Naval and Military Authorities and the medical profession from the experience of the war with a view to recording for future use the ascertained facts as to the origin, nature and remedial treatment of "shell shock," and as to whether by military training or education some scientific method of guarding against its occurrence could not be devised.

In a brief note on this report, it is scarcely necessary to enter into a consideration of the more purely military aspect of this subject, but a summary of the medical findings may not be without interest.

It was agreed that "shell shock" had been a gross and costly misnomer, and that the term should be eliminated from the nomenclature. The war produced no new nervous disorders, all those which occurred had previously been recognized in civilian practice. Owing to the special circumstances of the war these disorders appeared in some cases in an aggravated form, and the numbers suffering from them were very large.

The cases divided themselves into three main groups: genuine concussion without visible wound; emotional shock, either acute or developing slowly as a result of prolonged strain and terrifying experience, the final breakdown being

sometimes brought about by some relatively trivial cause; and nervous and mental exhaustion the result of prolonged strain and hardship. In many cases, however, the three factors of commotional and emotional shock and exhaustion were combined in varying proportions.

Many points of interest have been brought to light and the verbatim evidence of witnesses is by no means the least instructive part of the report. Here will be observed personal experiences bearing upon the psychology of fear, upon cowardice, upon malingering, upon the influence of war stress in the production of insanity, and valuable recommendations upon the prevention of "shell shock."

The treatment of the neuroses observed in soldiers is considered in detail, and the several forms of psychotherapy are commented upon with fairness and discretion.

The report may have a much wider significance than was intended when the idea of an inquiry was broached, as it deals with psychological problems which are not confined to war conditions.

Remembering and Forgetting. By T. H. PEAR. Methuen. Price 7s. 6d.

The analysis of dreams has been described as the royal road to the understanding of the unconscious. If we broaden the issue by substituting memory for dreams we will find that it becomes the nuclear problem of modern psychology, the full appreciation of which can only be obtained by the analysis of Memory and Forgetting.

This is the task that Professor Pear has undertaken in his book, designed primarily for the interested layman and the medical man who is interested in the psychological problems of medicine.

Being engaged in the elucidation of the experimental and theoretical problems of normal psychology, Professor Pear has not approached the subject in the manner of the psycho-analyst—that, is by plunging directly into the concrete details of the mental life—but begins by an analysis of memory processes from their genesis at the perceptional level, to the formation of after-sensations; thence to visual, auditory and kinæsthetic imagery, and ultimately to the formation of generic images upon which our ideas are based. This prepares the way for a consideration of the dream-life. The Freudian conception is fully considered, as well as the additions to it made by Rivers. He ends his analysis by a chapter on forgetting, which in the light of modern theory is the justification of all the preceding chapters.

There are one or two features of the author's method which make his treatment of the subject somewhat insufficient. Firstly, his own annoying visual imagery makes the subject appear easier than it actually is, although he does not fail to emphasize the importance of kinæsthetic imagery; and secondly the insufficient stress laid in the earlier chapters on dreams on the affective tone of the memories in dreams.

The two essays on synæsthesia and number forms are important for the psychology of imagery, and have an indirect bearing on the subject of remembering.

The whole book would well repay reading even to those engaged in applied psychology, for it deals with the theoretical basis of memory. It is written in a clear and succinct style.

Suggestion and Mental Analysis. By WILLIAM BROWN. Pp. 165. University of London Press. 1922. Price 3s. 6d.

The author is of the opinion that the two main forms of psychotherapy, that is suggestion and mental analysis, are not mutually exclusive as the extreme partisans of each system maintain. The aim of this small book is to give an elementary and non-technical account of their relations to one another, and to show that by harmonizing them as far as possible a sound system of psychotherapy can be built up.

The earlier chapters form a concise and in the main a sufficient introduction to the subject for the layman and non-specialist for whom the book is written, while the last three deal chiefly with Bergson's philosophy and the relation it bears to the author's own views.

Though written in a simple and clear style the book lacks the cohesion so necessary in an elementary text-book.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I to XXIII inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.